PUBLIC HEALTH REPORTS

VOL. 53 SEPTEMBER 16, 1938 NO. 37

INCIDENCE OF RHEUMATIC HEART DISEASE AMONG COLLEGE STUDENTS IN THE UNITED STATES

Based on Replies to a Questionnaire [1]

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Rheumatic heart disease is the most common form of heart disease among persons of college age, accounting for at least 90 percent of detectable structural changes, notably valvular disease, cardiac enlargement, and adherent pericardium. Congenital cardiovascular malformations and idiopathic enlargement account for most of the remaining cases. Adherent pericardium from tuberculosis, pneumonia, septic infections, or of unknown etiology is occasionally encountered. It is doubtful, however, whether many persons suffering from these conditions reach college. Although elevation of the arterial blood pressure is not uncommon among persons of college age, structural changes from this cause cannot usually be detected during this age period.

Wood (*1*), at the University of Pennsylvania, found 31 cases of rheumatic heart disease among 3,086 students, an incidence of 10 per 1,000. Paul (*2*), at Yale, reported 65 cases among 7,914 students, or 8.2 per 1,000. With these exceptions, the recent literature seems singularly devoid of studies of rheumatic heart disease among students attending institutions of higher education. College students constitute a fairly homogeneous group from which it should be possible to obtain information of epidemiological significance.

REPLIES TO QUESTIONNAIRES AND PARTICIPATING INSTITUTIONS

Inquiries concerning the incidence of rheumatic heart disease were sent to 213 colleges and universities with enrollments of at least 500 students. Replies were received from 87 institutions. Two indicated less than 100 physical examinations each and were discarded. The University of Pennsylvania was unable to furnish information for the year under study on account of an arrangement whereby town students are given only preliminary physical examinations and then referred to their family physicians. The study by Dr. F. C. Wood at

[1] From the Office of Heart Disease Investigations, National Institute of Health, branch office, 133 South 36th St., Philadelphia, Pa.

the University of Pennsylvania, made in 1931–32, was included, so that altogether reports were available from 86 colleges and universities.

The following institutions participated in this study: Adelphi College, Alabama College, Albright College, Alfred University, University of Arkansas, Beaver College, Berea College, Brigham Young University, Brown University and Pembroke College, Bryn Mawr College, Bucknell University, Carleton College, Carnegie Institute of Technology, University of Chicago, University of Cincinnati, Claremont College, Colorado College, Colorado State College, Columbia University, Connecticut State College, Cornell University, Davidson College, Denison University, University of Denver, University of Detroit, University of Florida, Fordham University, Gonzaga University, Hamilton College, Hampton Institute, University of Hawaii, Hollins College, Hunter College, University of Idaho, University of Illinois, University of Iowa, Johns Hopkins University, University of Kansas, Kent State University, Lafayette College, Loyola University, Loyola University of Chicago, Massachusetts State College, Miami University, Michigan State College, University of Michigan, University of Minnesota, University of Missouri, State University of Montana, Mount Holyoke College, University of Nevada, University of New Hampshire, North Carolina State College, Woman's College of the University of North Carolina, Oberlin College, Ohio State University, Ohio Wesleyan University, Oklahoma Agricultural and Mechanical College, Oklahoma College for Women, Pennsylvania State College, University of Pennsylvania, Princeton University, College of Puget Sound, Randolph Macon Woman's College, Redlands University, Rhode Island State College, Rice Institute, University of Richmond, University of San Francisco, South Dakota State College, Southern Methodist University, Stanford University, Syracuse University, University of Tennessee, Agricultural and Mechanical College of Texas, Texas State College for Women, Tufts College, University of Utah, Vanderbilt University, University of Vermont, Washington State College, West Virginia University, College of William and Mary, University of Wisconsin, University of Wyoming, and Yale University.

The writer wishes to acknowledge his appreciation to the directors of student health services and administration officers of these educational institutions for their cooperation.

INCIDENCE BASED ON REPLIES TO QUESTIONNAIRE

Among 104,163 student health examinations, 1,207 cases of rheumatic heart disease, an incidence of 11.6 per 1,000 physical examinations, were reported. Among 63,828 men students, 607 cases were reported, giving a rate of 9.5 per 1,000, while among 40,335 women

students 600 cases were reported, or 14.9 per 1,000. Of the 86 colleges and universities, 59 reported on examinations of men and women students, 16 only on men students, while 11 were strictly women's colleges. Altogether 75 institutions reported on physical examinations of men students and 70 reported on women students. The total enrollment of these institutions was 295,513 students.

TABLE 1.—*Incidence of rheumatic heart disease among 104,163 student health examinations in 86 universities and colleges in the United States on the basis of sex, size of institution, and with or without affiliated medical schools*

	Number of colleges and universities	Total number of students examined	Number of cases of rheumatic heart disease	Rate per 1,000 examinations
Total number	86	104,163	1,207	11.6
Total males	75	63,828	607	9.5
Total females	70	40,335	600	14.9
Colleges and universities reporting less than 500 examinations	27	8,758	170	19.4
Colleges and universities reporting 500 to 1,000 examinations	28	18,917	300	15.9
Colleges and universities reporting 1,000 to 2,000 examinations	19	27,869	298	10.7
Colleges and universities reporting over 2,000 examinations	12	48,619	439	9.0
Institutions with affiliated medical schools	22	50,307	346	6.9
Large universities with medical schools in selected group	14	46,098	296	6.4

The reported incidence of rheumatic heart disease bore an inverse relationship to the number of student health examinations performed (table 1). The incidence in institutions reporting less than 500 examinations was 19.4 per 1,000, among those reporting 500 to 1,000 examinations the rate was 15.9 per 1,000, among those reporting 1,000 to 2,000 student health examinations the rate was 10.7 per 1,000, while in the larger schools reporting over 2,000 physical examinations the incidence was only 9.0 per 1,000. This incidence relationship was also noted when the total enrollment of the institutions was used as a basis for comparison.

The incidence in universities with affiliated medical schools was notably less than in the 86 colleges and universities as a whole, and decidedly less than in the colleges and universities without medical school affiliation. Among 22 universities with medical schools giving 4-year courses, in a total of 50,307 student health examinations, 346 cases of rheumatic heart disease were reported, a rate of 6.9 per 1,000. Among 53,856 physical examinations at 64 other institutions, 861 cases of rheumatic heart disease were reported, or 16.2 per 1,000. In only two instances were rates greater than 20 per 1,000 reported from universities with medical schools. In both of these less than 1,000 examinations were performed.

TABLE 2.—*Reported incidence of rheumatic heart disease on student health examinations in 14 large universities with affiliated medical schools, reporting at least 1,500 student health examinations, whose student health services are members of the American Student Health Association*

University	Total number of student examinations	Number of cases of rheumatic heart disease	Rate per 1,000 examinations
Stanford University	1,740	10	5.8
Yale University	5,027	23	4.6
University of Chicago	1,841	10	5.4
University of Illinois	4,662	41	8.8
University of Iowa	1,649	3	1.8
University of Michigan	3,485	19	5.5
University of Minnesota	5,028	5	1.0
University of Kansas	1,616	14	8.7
Syracuse University	1,746	9	5.0
Cornell University	5,840	46	7.9
Ohio State University	4,361	25	5.7
University of Tennessee	2,397	20	8.3
University of Wisconsin	3,620	40	11.0
University of Pennsylvania [1]	3,086	31	10.0
Total	46,098	296	6.4

[1] Figures taken from a study made by Dr. F. C. Wood during 1931-32.

In table 2 are shown the results from a selected group of 14 large universities with affiliated schools of medicine, reporting at least 1,600 student health examinations, whose student health services are members of the American Student Health Association. Among 46,098 student health examinations, 296 cases of rheumatic heart disease were reported, a rate of 6.4 per 1,000. In no instance did the incidence exceed 11.0 per 1,000. It is believed that this rate of 6.4 per 1,000 nearly approximates the true incidence of rheumatic heart disease among college students, since these institutions have well organized health services and are in better position to avail themselves of the services of consultants and modern diagnostic equipment.

The reported incidence of rheumatic heart disease ranged from no cases in 3 institutions to as high as 62 per 1,000 students (table 3). This could not be accounted for on the basis of geographic location, since few schools from the deep South participated in this study. The rates were not higher in urban universities than in institutions located in smaller centers of population, or in State universities which draw heavily from small towns and rural areas. The unusually high incidences were reported more commonly from strictly women's colleges than from men's colleges or coeducational institutions. Among 13,024 health examinations in women's colleges the reported incidence was 21.0 per 1,000, while among 27,311 examinations performed on women students in coeducational institutions the rate was only 11.9 per 1,000.

TABLE 3.—*Frequency distribution of the reported incidence of rheumatic heart disease in 86 colleges and universities in the United States*

Rate per 1,000 examinations	All colleges and universities	Institutions reporting examinations on male students	Institutions reporting examinations on women students
0 to 9.9	45	40	37
10 to 19.9	21	19	13
20 to 29.9	7	9	8
30 to 39.9	8	2	6
40 to 49.9	2	0	3
50 to 59.9	2	5	1
60 and over	1	0	2

Based on 104,163 student health examinations (table 1) the reported incidence of rheumatic heart disease among men students was 9.5 per 1,000, while that among women students was 14.9 per 1,000. Since a number of factors, such as the size of the institution, number of health examinations performed, medical school affiliation, and whether the examinations among women were reported from women's colleges or coeducational institutions enter into these determinations, these rates cannot be taken at their face value. In 59 coeducational institutions the rate among 53,068 physical examinations on men students was 9.0 per 1,000, while among 27,311 female students it was 11.9 per 1,000. In 29 of these institutions the rate reported was higher among men students, in 28 it was higher among women students, while in two the rates were practically the same.

The incidence among 32,863 male students in the 14 large universities with affiliated medical schools was 6.0 per 1,000, while among 13,235 women students it was 7.4 per 1,000. In one large university, probably due to some local condition, the rate among women students was nearly 21 per 1,000. When this university is excluded, the rate among men students is 6.3 per 1,000, while that among women students is 6.0 per 1,000. The reported rates among men students exceeded those among women in five of these universities, the opposite was true in seven instances, in one university the rates were about equal, while one institution reported only on men students. It is extremely doubtful whether sex plays an important role in the incidence of rheumatic heart disease among college students.

All of the 86 colleges and universities indicated that students disrobed to the waist for purpose of physical examination. This is in happy contrast to the fact that in several States, including some of the most populous and otherwise progressive, there are still laws against disrobing school children to the waist for health examinations in the public schools.

RHEUMATIC HEART DISEASE AS A STUDENT HEALTH PROBLEM

Rheumatic heart disease presents a definite, but limited, problem among student bodies in institutions of higher education. Every effort should be made to detect this condition during entrance and periodic health examinations, and to estimate the extent of functional impairment. It may not only be necessary to proscribe certain forms of competitive athletics and to modify the physical education program, but the entire curriculum of a student may have to be changed. Prudence demands that a student be tactfully advised against undertaking a course of study leading to a career too strenuous for his handicap.

Student health examinations should be made as much for the purpose of ruling out functional abnormalities as to detect organic disease. The concept of preventive medicine is a comparatively recent one to most persons. The public, students included, is inclined to misdirect its fears on matters pertaining to personal health. Many otherwise well-informed people receive most of their health instruction through the medium of commercial advertising—in the press, over the air, by hand bills and bill boards, and through the mails. This material is highly biased, almost never authoritative, and often false.

The public is more afraid of heart disease than of any other common condition, with the exception of cancer. Cabot (*3*) states that nearly 10 percent of Harvard freshmen in one class examined by Dr. Roger I. Lee believed that they had a "weak heart" or some more definite evidence of heart disease. While the failure to diagnose heart disease may lead to serious consequences, the diagnosis of a functional murmur as heart disease may be nearly as unfortunate. Not only may the student forego many pleasurable and useful activities in college, but his entire career may be influenced. The specter of heart disease is nearly always a source of mental anguish to the individual and his family, enhanced because of the readiness with which the public associates heart disease with sudden death.

Among the symptoms of disease, apprehension is the common denominator. All patients are more or less fearful; else they would not consult a physician. The student health physician should approach each case with an open mind. Young adults often grow up with the delusion that they have organic heart disease, frequently based on a diagnosis of heart disease or chance remark about a murmur by a physician while attending an intercurrent disease or during a school medical inspection. Firm in the belief that there is something wrong with their hearts many fail to be reexamined. By the time they reach adult life it is often difficult to disabuse them of the belief. A painstaking history and physical examination, together with such laboratory procedures as are available, followed by a reassuring and sympathetic

talk, the correction of defects or habits which give rise to heart consciousness, and encouragement to greater physical effort, will usually suffice. Sometimes mild sedatives are useful. In the more severe cases the mental hygienist may be of service.

Even when rheumatic heart disease is suspected or detected, care should be maintained not to alarm unduly. A quiet talk will do much to dispel fears. To restrict the student too much may result in the superimposition of a cardiac neurosis on a very minor form of heart disease. The neurosis may become the more troublesome factor. Each case requires individual management. The actual treatment should be left to the family physician. The primary aim of the college physician should not be to restrict the student from engaging in useful and pleasurable activities, but to determine the extent to which he can safely participate.

In attempting to evaluate rheumatic heart disease, as much attention should be paid to the question of rheumatic activity as to the valve lesions. Although rheumatic heart disease is not as likely to be accompanied by signs of active infection in this age period as in childhood, when signs of infection occur, rest in bed is indicated. Persons with mitral stenosis, aortic insufficiency, or adherent pericardium should refrain as a safety measure from strenuous competitive athletics regardless of their functional capacity at that time, as also should cases of mitral insufficiency with signs of cardiac enlargement. Individuals with histories of rheumatic infection in childhood and with systolic apical murmurs not showing signs of cardiac enlargement and who have not had recent rheumatic infection need not curtail their physical activities to any great extent, but it is usually advisable that they do not participate in the more strenuous sports. Their cardiac condition should be observed from time to time. Where there is doubt concerning the presence of cardiac enlargement, it is better to err on the side of safety.

COMPARISON OF RHEUMATIC HEART DISEASE WITH PULMONARY TUBERCULOSIS AS A STUDENT HEALTH PROBLEM

Rheumatic heart disease is not as important a problem among college students as is pulmonary tuberculosis. Few cases of rheumatic heart disease actually develop in students while in college. There is not the same danger of transmission of rheumatic heart disease in institutions as there is of tuberculosis. Neither of these diseases is as common among college students as in similar age groups in the general population.

One of the most striking contrasts between these diseases is in the manner of detecting them in large groups, such as student bodies. In tuberculosis, the responsible microorganism is known, and it is pos-

sible, by means of the tuberculin test, to determine who has been infected. By X-raying either the positive reactors or the entire student body, adult type pulmonary tuberculosis can be detected by a highly efficient objective method at a stage before auscultatory signs have developed. The more carefully the disease is sought for, the oftener it is diagnosed. In 4 colleges (*4*) without adequate programs for case finding in 1932–33, among 15,374 student health examinations, 11 cases of pulmonary tuberculosis were detected, giving a rate of 0.7 per 1,000. In 7 colleges with adequate methods for case finding, among 38,392 student health examinations during the same year, 262 cases of adult type pulmonary tuberculosis were found. Nearly 10 times as many cases of pulmonary tuberculosis were discovered, and at earlier stages, in institutions using approved methods and equipped with the proper diagnostic armamentaria, as in colleges without definite plans for case finding.

The situation is entirely different with regard to the determination of rheumatic heart disease among members of student bodies. There is no method of "screening" suspected cases comparable to the application of the tuberculin test, nor is there an impersonal objective means for detecting rheumatic heart disease with the accuracy of the X-ray film for detecting pulmonary tuberculosis. The tendency in mass diagnosis of rheumatic heart disease is toward over-diagnosis. In sharp contrast to pulmonary tuberculosis, the greater care exercised in the diagnosis of rheumatic heart disease, the fewer cases are found. Trained cardiologists are, as a rule, less likely to diagnose rheumatic heart disease than are physicians who encounter cardiac abnormalities less frequently.

SUGGESTIONS FOR IMPROVING DIAGNOSIS OF RHEUMATIC HEART DISEASE, ESPECIALLY IN INSTITUTIONS WITHOUT AFFILIATED MEDICAL SCHOOLS

It is not the purpose of this discussion to review at great length the physical signs indicative of rheumatic heart disease in presumably healthy young adults, the methods for eliciting them, or the pitfalls in the interpretation of these signs. A number of recent textbooks on heart disease furnish this information in descriptive detail. So far as possible, the diagnostic criteria of the American Heart Association should be followed (*5*).

So much is dependent on the ability, interest, and training of the examiner that it is difficult to lay down hard and fast rules. In the larger universities, especially those with affiliated medical schools, the problem of diagnosis is somewhat simplified. The health services are usually well organized and have access to diagnostic equipment and the services of consultants.

Difficulties in diagnosis are increased in the smaller colleges and universities. Wherever possible, these institutions should avail themselves of the services of a competent cardiologist or internist to pass on questionable cases and to appraise the functional capacity of known cases, or should require the student to obtain an opinion from a qualified consultant. Even this suggestion is to a large extent a counsel of perfection. In many places these services are not available or cannot be obtained for financial reasons. It often devolves upon the college physician to make the decision concerning the presence or absence of heart disease.

Too much emphasis can hardly be placed on the past and present medical history in the diagnosis of rheumatic heart disease. A past history of rheumatic fever or chorea can be obtained in about 75 percent of rheumatic heart disease in early adult life. An inquiry should be made concerning tonsillitis, although this is more difficult to evaluate. "Growing pains" severe enough to be remembered, are often significant. While chorea without rheumatism apparently causes heart disease much less frequently, it is not usually possible to be certain of a past history of "pure" chorea when dealing with young adults. It is also important to ascertain whether there have been bouts of active carditis without a rheumatic history or subsequent to an attack of rheumatic fever. Histories of prolonged illness not otherwise accounted for should be thoroughly investigated. A positive familial history of rheumatic heart disease should be given weight in making a diagnosis.

Of equal importance is the question of functional capacity. Has the student been able to participate in athletic competition? Does ordinary exertion cause undue dyspnea or fatigue? In interpreting the answers to these questions consideration must be given the student's constitution, outlook on life, and his scholastic and athletic aspirations.

According to Grant (*6*), 2 percent of the student body at Dalhousie University, in Canada, gave histories of rheumatic fever, while 0.5 percent gave histories of chorea. Many persons with histories of rheumatic infection show clear-cut evidence of rheumatic heart disease, while others do not show signs suggesting this condition. There is a borderline group which have faint systolic mitral murmurs. These are sometimes difficult to evaluate. Without the history of rheumatic infection, these conditions would usually be regarded as functional. Again it is necessary to go into the question of functional capacity and rheumatic activity quite carefully. It is difficult to escape the conclusion that in many instances the murmurs are due to minor residual changes in the mitral valve. It is better in most cases to consider them as potential cases of rheumatic heart disease and to observe them from time to time, but not to label them as definitely having organic heart disease.

The era has long passed (if it ever existed) when any but the most obvious forms of heart disease could be diagnosed by the ceremonial laying on of a stethoscope. Intelligent conclusions cannot be reached by lining the student body up and attempting to detect heart disease by a cursory auscultation as students march past. On the other hand, the diagnosis of rheumatic heart disease can usually be made during the course of a painstaking physical examination, without resort to special instruments such as the electrocardiograph or X-ray equipment. By means of a careful physical examination it is often possible to discover important diagnostic signs which would otherwise be overlooked.

The cardiac examination should be part of a general physical examination conducted in a quiet room with the student disrobed to the waist. It should be done thoroughly, but need not be time consuming. After the pulse and arterial blood pressures have been determined, the precordium should be palpated for thrills and to locate the apex impulse. At the same time the neck should be examined for abnormal pulsations. Although the position of the apex impulse is usually a better criterion of enlargement, the heart should be percussed to determine cardiac displacement and to confirm the impressions concerning its size. The heart should then be auscultated with the subject in the upright, recumbent, and left lateral position, both before and after sufficient exercise to accelerate the heart rate. Undue acceleration to moderate exercise should be noted. The routine determination of cardiac rates and arterial blood pressures for a given number of minutes after set exercises rarely affords information of interpretable value.

Efforts should be made to determine noncardiac causes for cardiac abnormalities, such as thyroid disorders, anemia, pulmonary tuberculosis, overindulgence or sensitivity to tobacco, coffee, or alcohol, tachycardias of neurogenic origin, and other factors.

During the past 20 years clinicians have come to rely more and more on instruments of precision in the diagnosis of heart disease. The widespread publication of information obtained from the study of electrocardiograms has been attended, to a certain extent, by unfortunate repercussions in that it has cast an aura of mystery around the diagnosis of heart disease. Sight is often lost of the fact that the workers who have done the most to advance clinical electrocardiography are among the first to recognize its limitations. While it is well to include an electrocardiographic report in cases of suspected or proved cases of organic heart disease for the sake of completeness where it is readily available or wherever clinical research is being undertaken, the electrocardiogram should not be regarded as the *sine qua non* in the diagnosis of rheumatic heart disease in young adults. Electrocardiograms infrequently furnish valuable assistance in the

diagnosis of inactive rheumatic valvular disease encountered among persons of college age.

The teleoroentgenogram and orthodiogram are more likely to furnish information of real significance in the diagnosis or evaluation of rheumatic valvular heart disease and should be included wherever possible. In many instances the knowledge derived is largely of academic interest, having little influence on the advice given the patient. Sometimes it is necessary to depend on radiography to determine cardiac enlargement or changes in contour, especially in connection with certain systolic apical murmurs. Here the diagnosis may in a large measure be dependent on X-ray visualization (*7*, *8*, *9*, *10*). In the opinion of the writer, roentgenography of the heart and large vessels is destined to play an increasingly important role in the diagnosis of cardiovascular diseases.

The tendency toward obtaining lower incidences of heart disease as a result of more careful examinations has been suggested in cardiac surveys of school children. Robey and his associates (*11*), on re-examining 2,311 Boston school children nominated by school physicians because of suspected cardiac abnormalities, were able to find definite evidence of organic heart disease in only 625 pupils in a school population of 119,337 persons. Cahan (*12*), in Philadelphia, among 33,293 graded and high-school students, found 191 cases of organic heart disease in 863 pupils referred by school physicians because of histories or physical findings suggesting heart disease. It is likely that in both of these instances the reported incidence of organic heart disease would have been higher had not the students been subjected to special examinations by experienced cardiologists. Since the prognosis of actual cases remains uninfluenced and of a series of cases is made relatively worse by the application of stricter criteria for diagnosis, the fact that fewer cases are found under these circumstances should not be interpreted as minimizing the effects of rheumatic heart disease on student bodies.

To a certain extent it is almost inevitable that higher incidences of heart disease be found in institutions whose student health departments do not have access to consultation services and diagnostic equipment requisite to the proper evaluation of questionable physical signs. A college physician is probably justified in many instances in refusing a student permission to engage in strenuous competitive sports when he finds a systolic apical murmur with possible cardiac enlargement. Insurance companies and civil and military authorities usually protect themselves by rejecting such cases. If after a careful physical examination with due emphasis on the past medical history the college physician is unable to make the diagnosis to his own satisfaction, he should place the matter squarely before the student and his parents with the suggestion that they obtain an opinion from

a competent cardiologist or internist, even though it entails a trip to the nearest medical center. The question of the presence or absence of heart disease is too important a matter to be left in doubt if it can be avoided.

SUMMARY

1. Among 104,163 student health examinations in 86 colleges and universities in the United States, 1,207 cases of rheumatic heart disease, a rate of 11.6 per 1,000, were reported. Among 63,828 men students, 607 cases, or 9.5 per 1,000, were reported, while among 40,335 women students 600 cases, or 14.9 per 1,000, were indicated.

2. The reported incidence of rheumatic heart disease showed an inverse relationship to the size of the college or university and the number of student health examinations reported.

3. In 14 large universities with affiliated medical schools reporting at least 1,500 student health examinations, and whose student health services are affiliated with the American Student Health Association, among 46,098 student health examinations 296 cases were reported—an incidence of 6.4 per 1,000.

4. It is doubtful whether sex is an important factor in the incidence of this disease among college students.

5. In contradistinction to adult type pulmonary tuberculosis, the reported incidence of rheumatic heart disease is lower in institutions with well organized health services. The problem in rheumatic heart disease is not primarily case-finding but the detection and interpretation of physical signs.

6. While it is suggested that persons with physical signs suggesting heart disease or having past histories of rheumatic infection be subjected to complete cardiovascular surveys, there is no objective method for the mass diagnosis of rheumatic heart disease comparable to tuberculin testing and X-raying the chest for the detection of adult type pulmonary tuberculosis. The diagnosis of rheumatic heart disease is dependent in a large measure on the interest, skill, and experience of the individual examining physician. For this reason, the services of well qualified consultants should be obtained wherever feasible to pass upon doubtful cases and to evaluate the functional status of known cases.

7. To a certain extent it is almost inevitable that more diagnoses of heart disease are made in smaller institutions. Even under the most favorable circumstances it is difficult to evaluate certain physical signs suggesting heart disease.

8. An unwarranted diagnosis of heart disease may seriously affect a student's career both in college and in later years. Painstaking examinations and kindly reassurance are necessary to dispel cardiac neuroses.

9. In the diagnosis of rheumatic heart disease it should be borne in mind that it is an acquired condition due to an infection. In most cases where a significant history and physical signs are indicative of this disease, the examination should be interpreted in the light of the past and present history of rheumatic infection, together with its influence upon functional capacity.

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SUSCEPTIBILITY OF MICE TO SPONTANEOUS, INDUCED, AND TRANSPLANTABLE TUMORS

A Comparative Study of Eight Strains*

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The genetic constitution of the test animal is known to be of considerable importance in experimental cancer. In this report, results of several experiments are recorded in which mice of highly inbred strains were tested for their reactions to certain carcinogenic hydrocarbons. The report is one of a series of publications dealing with the response of these strains to injections with carcinogens or to inoculations with

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transplantable tumors, while at the present time the incidence of spontaneous tumors is being determined. The primary object of this work is to ascertain the outstanding characteristics of the various strains when subjected to certain experimental procedures so that in the future it will be known which strain will supply the most suitable test animals for problems in the field of experimental cancer. In the discussion of this communication the outcome of this entire series of investigations is summarized.

The influence of heredity in the induction of tumors in experimental animals has received attention from investigators in various laboratories. Curtis and Bullock (*19*) found strain differences in susceptibility to induced Cysticercus sarcoma of the rat's liver. Lynch (*24*), Kreyberg (*22*), and Korteweg (*21*), as well as Reinhard and Candee (*28*), have shown that strains of mice vary in their susceptibility to tar-induced skin tumors. Reinhard and Candee and also Kreyberg detected sex influence in susceptibility to tar painting. Experimental evidence has been presented by Branch (*17*), Boyland and Warren (*16*), Dobrovolskaïa-Zavadskaïa (*20*), Lynch (*25*), and from this laboratory (*1, 2, 11*) which shows that different strains of mice vary in their susceptibility to the cancer-inducing power of carcinogenic hydrocarbons.

EXPERIMENTAL ANIMALS

Eight inbred strains of mice, which are described below, were used in the investigations. When specific references are not given regarding the incidence of spontaneous mammary tumors, the information was obtained from the List of Stocks supplied by the Roscoe B. Jackson Memorial Laboratory.

Strain C_3H.—This strain was originated in 1920 by Strong (*31*). Published reports by Strong (*31*), Bittner (*14*), and from this laboratory (*6*) show that the breeding females have a high incidence of mammary tumors. Recently it has been found (*12*) that the nonbreeding females also have a high incidence of mammary tumors. The incidence of other growths has not been recorded, but spontaneous lung and liver tumors have been found in a colony of the strain which is being propagated in this laboratory.

Strain C.[1]—This strain was originated by MacDowell. It was originally derived from Bagg's albinos and has been inbred for more than 40 generations. There are no published accounts of the incidence of spontaneous tumors in this strain, but Dr. G. D. Snell, of the Bar Harbor Laboratories, has kindly supplied the following provisional information in a personal communication: The breeding females show a low incidence (below 5.0 percent) of mammary tumors,

[1] It is understood that the final designation for this strain has not been decided.

and the lung tumor incidence is approximately 20 to 30 percent. Internal tumors, probably lymphoblastomas, are the most common with an incidence of over 50 percent.

Strain C57 black.—This strain (*27*) has been inbred since 1921 and is noted as a strain in which the breeding females have a very low incidence (less than 1.0 percent) of mammary tumors under normal breeding conditions. The incidence of other tumors has been reported by Cloudman, Bittner, and Little (*18*).

Strain M "Leaden."—Inbred since 1921. The breeding females exhibit a "medium to low" incidence of mammary tumors. The incidence of other tumors is not known.

Strain A.—Originated by Strong (*32*) in 1921. Reports by both Strong (*30*) and Bittner (*13*) show that the breeding females have a high incidence of mammary tumors. Bittner (*15*) has found that many of these mice develop spontaneous pulmonary tumors, and Cloudman, Bittner, and Little (*18*) have recorded the incidence of other types of tumors.

Strain D.—Originated in 1909 by Little and is better known as the "Little dilute browns." Murray (*26*) has published a comprehensive study of the strain showing that the breeding females have a high incidence of mammary tumors, but the incidence of other tumors has not been recorded.

Strain I.—This strain was originated in 1927 by Strong. No published accounts of the incidence of spontaneous tumors are on record, but experience with the strain in this laboratory suggests that the breeding females develop few mammary tumors. It has been found (*10*) that the mice develop a pronounced hyperplasia of the epithelium in the pyloric portion of the stomach which eventuates in death at a relatively early age.

Strain Y.—The origin of this strain has been described by Little (*23*). The mice have been inbred for at least 10 years, and the incidence of mammary tumors is given as "medium." The incidence of other tumors has not been reported.

In the experiments to be described here, mice of strains A and M were obtained from the Roscoe B. Jackson Memorial Laboratory. Mice of the other six strains were raised in this laboratory, where the strains are being propagated. The diet consisted of Purina dog chow, and an unlimited supply of water was available at all times. Only virgin mice were used in these investigations.

EXPERIMENTAL OBSERVATIONS

A series of experiments has been performed to determine the susceptibility of the various strains to subcutaneous injection of carcinogenic hydrocarbons. Some of the results have been published in

previous papers; and in this report four more experiments will be recorded, since they are typical of others along the same lines.

EXPERIMENT 1

In this investigation 3-month-old mice of strains C_3H, C, and I were injected subcutaneously in the right axilla with 0.2 cc of a lard solution of 1:2:5:6-dibenzanthracene which contained 0.8 mg of the hydrocarbon. The injections were made on February 5, 1937, and the first tumor appeared in a C_3H mouse on April 29, 1937. In this experiment, as in all subsequent experiments recorded, the mice were examined each week for the presence of induced tumors. All mice which developed tumors or died from other causes were examined post mortem. The experiment was discontinued on January 7, 1938, when all surviving mice were killed and examined. The experiment is summarized in table 1.

TABLE 1.—*Experiment 1: Summary of an experiment in which each mouse received a single subcutaneous injection of 0.8 mg of 1: 2: 5: 6-dibenzanthracene in 0.2 cc of lard*

Time in weeks			12	16	20	24	28	32	36	40	44	45				
Strain	Sex	Number of mice injected	Number of tumors										Total number of tumors	Average time in weeks	Number dying without tumor	Number killed Jan. 7, 1938
C_3H	M	15	2	3	7	3	----	----	----	----	----	----	15	17.8	0	0
C	F	17	----	2	----	4	4	1	----	1	1	----	13	23.8	1	3
I	F	22	----	----	1	2	3	4	2	----	1	1	14	30.6	1	7
I	M	22	----	----	2	1	2	----	----	1	2	----	8	31.5	5	9

In table 1 it is seen that strain C_3H mice developed tumors earlier than the other strains and that strain I mice were the most resistant to the carcinogenic agent. It is essential to mention that, while the time of appearance of the induced tumors is listed in the table by periods of 4 weeks, the figures in the sixth column, which represents the average time in which the tumors occurred, were computed from the number of new tumors observed each week. This procedure is followed in other tables of this report.

Autopsy findings as regards lung tumors in this experiment were of special interest. Of the 13 strain C mice which developed subcutaneous sarcomas at the site of injection, 9, or 69 percent, had one or more primary lung nodules, while of the 22 strain I mice, 9, or 40 percent, had developed lung nodules. There were 3 strain C and 16 strain I mice killed on January 7, 1938, when the experiment was terminated. All these were tumor free at the injection site, but all of strain C and 13 of the strain I animals had developed lung tumors.

The results of the experiment show that the C_3H mice were the most susceptible and the strain I mice the most resistant to subcutaneous tumors induced by the hydrocarbon, and that both the C and I mice developed lung nodules following subcutaneous injection of the carcinogen.

EXPERIMENT 2

Mice of strains C, C57 black, M and A, all of which were 3 months old, were injected subcutaneously in the right axilla with lard solutions of 1:2:5:6-dibenzanthracene or methylcholanthrene on March 11, 1937. Each animal received 0.8 mg of one of the hydrocarbons dissolved in 0.2 cc of lard. The experiment ended on January 7, 1938, when all mice free from induced tumors at the injection site were killed. The purpose of the experiment was to determine the relative susceptibility of the strains of mice to both hydrocarbons and to detect any sex difference in susceptibility. The experiment is summarized in table 2.

Table 2 reveals that no particular strain was very susceptible or resistant to the cancer-inducing hydrocarbons. These four strains of mice are included in a group designated as of intermediate susceptibility and will be discussed later in this paper.

TABLE 2.—*Experiment 2: Time of appearance of subcutaneous tumors in mice of four strains following the injection of 0.8 mg of 1: 2: 5: 6-dibenzanthracene or methylcholanthrene dissolved in 0.2 cc of lard*

Time in weeks				8	12	16	20	24	28	32	36	40	44				
Strain	Sex	Compound injected[1]	Number of mice injected	Number of tumors										Total number of tumors	Average time in weeks	Number dying without tumor	Number killed Jan. 7, 1938
C	F	MCA	11	---	4	1	1	1	---	---	1	---	---	8	16.3	1	2
C	M	MCA	21	---	7	3	5	3	---	---	1	---	---	19	16.7	0	2
C	F	DBA	11	---	---	---	1	3	1	1	1	---	1	8	27.0	0	3
C	M	DBA	20	---	---	1	7	3	2	1	---	2	---	16	22.2	2	2
C57 black	F	MCA	21	---	2	3	3	3	1	4	---	---	1	17	22.5	1	3
C57 black	M	MCA	12	---	2	6	1	---	---	2	---	---	---	11	17.2	0	1
C57 black	F	DBA	22	---	---	2	---	2	4	2	5	1	---	16	28.3	4	2
C57 black	M	DBA	12	---	---	3	3	---	1	---	---	---	---	7	18.0	0	5
M	F	MCA	12	---	4	3	---	2	---	---	---	---	---	9	14.3	1	2
M	M	MCA	11	1	---	3	1	2	1	---	---	---	---	8	17.9	0	3
M	F	DBA	12	---	---	1	1	1	3	2	---	1	---	9	26.4	3	0
M	M	DBA	11	---	---	---	4	1	4	---	---	1	---	10	24.2	1	0
A	M	MCA	12	---	5	4	1	---	---	---	---	---	---	10	14.0	2	0
A	M	DBA	12	---	---	1	1	3	2	1	---	---	---	8	26.7	2	2

[1] MCA=methylcholanthrene; DBA=1: 2: 5: 6-dibenzanthracene.

However, there were several points of interest revealed by the experiment. In all the strains methylcholanthrene proved to be the more potent carcinogenic agent as shown by the average time in which the tumors appeared. But it is seen that in some mice of every strain 1:2:5:6-dibenzanthracene induced tumors earlier than did methyl-

cholanthrene, which indicates considerable individual variation in susceptibility although the animals were from highly inbred strains.

Autopsy findings confirmed the observations made in experiment 1 concerning lung tumors in strain C mice. Of the 27 mice which developed tumors following injection of methylcholanthrene, 6 had primary lung nodules; and of the 24 in which tumors were produced by 1:2:5:6-dibenzanthracene, 12 had primary growths within their lungs. Of the 4 methylcholanthrene-injected and 5 dibenzanthracene-injected mice killed on January 7, 1938, 2 of each group had lung growths. All of the strain A mice in the experiment had multiple lung nodules while such growths were not found in the C57 black or M mice.

So far as any sex difference in susceptibility was concerned, the results in the C57 black mice gave some indication that the females were more resistant than the males. It is believed that the question of variation in susceptibility due to sex should be mentioned with caution, for experience has revealed that the results of a single experiment may be misleading. However, the sex difference in susceptibility to subcutaneously injected hydrocarbons in C57 black mice has appeared repeatedly. The response of mice of this strain to solutions of methylcholanthrene or 1:2:5:6-dibenzanthracene in 4 experiments is summarized in table 3. The table includes the mice injected in experiment 2. In table 3 the numbers of new tumors found are listed according to the sex of the animal in which they arose. Just below these figures, and in heavy face type are the accumulated percentages of the total number of mice of each sex developing subcutaneous tumors.

TABLE 3.—*Summary of four experiments in which female and male mice of strain C57 black were injected subcutaneously with lard solutions of carcinogenic hydrocarbons*

Time in weeks					10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42		
Number of experiments	Amount of hydrocarbon injected	Sex	Number of mice injected	(a) Number of new tumors and (b) accumulated percentage of mice with tumors																		Total number of tumors	Died or killed without tumor
1	0.8 mg of methylcholanthrene.	F	20	*a*	--	2	1	2	1	2	1	2	1	--	3	1	--	--	--	--	1	17	8
				b	--	10	15	25	30	40	45	55	60	--	70	80	--	--	--	--	85		
1	do	M	12	*a*	2	--	4	2	--	1	--	--	--	--	--	--	2	--	--	--	--	11	1
				b	16	--	50	66	--	75	--	--	--	--	--	--	91	--	--	--	--		
3	0.8 mg of 1:2:5:6-dibenzanthracene.	F	43	*a*	--	--	2	3	1	1	2	6	5	2	2	2	3	2	--	1	--	32	11
				b	--	--	5	11	14	16	21	35	46	51	56	60	67	72	--	74	--		
3	do	M	42	*a*	--	--	1	4	10	2	3	3	6	1	3	--	--	--	--	--	--	33	9
				b	--	--	3	12	35	40	47	54	69	71	79	--	--	--	--	--	--		

Table 3 reveals that the males developed tumors earlier than did the females, which suggests that the males were more susceptible. In a previous report (4) an experiment was described in which hybrid

mice, derived by crossing strains C57 black and A, were injected subcutaneously with a lard-dibenzanthracene solution, and the carcinogen induced tumors earlier in the male than in the female mice. The figures presented in table 3 may be of some significance in the interpretation of the results attending injection of the hybrid mice. It should be mentioned that Reinhard and Candee (*28*), as well as Kreyberg (*22*), found that skin tumors induced by tar painting appeared earlier in female mice, and Branch (*17*) found no significant difference in tumor formation between C57 black males and females following skin painting with 1:2:5:6-dibenzanthracene.

EXPERIMENT 3

In this experiment 2-month-old mice of strains C_3H, A, I, and Y were injected subcutaneously in the right axilla with 2 mg of methylcholanthrene dissolved in 0.25 cc of lard. The purpose of the investigation was to determine whether the strain differences in susceptibility could be detected when a large amount of a powerful carcinogen was used. Mice of strain C_3H represented a very susceptible strain, and mice of strains I and Y were known to be very resistant to smaller amounts of carcinogenic hydrocarbons. Strain A mice were used as representatives of a strain regarded as of intermediate susceptibility to subcutaneous injection and also to determine the relative susceptibility of the lungs of strains A and I mice to induced tumors. The injection was given on September 10, 1937, and the experiment was discontinued on March 8, 1938, when all surviving mice were killed and autopsied. The results are presented in table 4.

TABLE 4.—*Experiment 3: Time of appearance of induced tumors in mice of strains C_3H, A, I, and Y following a subcutaneous injection of 2 mg of methylcholanthrene dissolved in 0.25 cc of lard*

Time in weeks			8	10	12	14	16	18	20	22	24	26				
Strain	Sex	Number of mice injected	Number of tumors										Total number of tumors	Average time in weeks	Number dying without tumor	Number killed Mar. 8, 1938
C_3H	F	29	10	8	2	----	----	----	----	----	----	----	20	8.7	0	0
C_3H	M	24	19	5	----	----	----	----	----	----	----	----	24	8.2	0	0
A	F	19	----	9	6	1	----	1	----	----	----	----	17	10.8	2	0
A	M	20	----	13	7	----	----	----	----	----	----	----	20	10.2	0	0
I	F	21	----	1	2	5	4	4	1	1	----	----	18	15.2	0	3
I	M	17	----	1	----	5	2	1	1	5	1	----	16	17.2	0	1
Y	F	19	----	----	----	2	3	1	1	1	----	3	11	18.7	6	2
Y	M	12	----	----	2	3	1	1	1	1	2	----	11	16.7	0	1

In table 4 it is seen that the amount of methylcholanthrene used in the experiment was not sufficient to overcome the strain differences in susceptibility; for, while the latent period was shortened in all strains, the mice of strain C_3H were considerably more susceptible

than those of strains I and Y, while strain A mice were of intermediate susceptibility. In most of the C_3H animals in this experiment a pronounced reaction was noted at the injection site as early as the fifth week after injection. This reaction consisted of a mass of soft tissue and was, apparently, the beginning of tumor development, for within another 2 or 3 weeks the masses had become hard and were found to consist of malignant tissue when examined microscopically. The figures in table 4 which denote the time of appearance of tumors in C_3H mice represent the time when the masses had hardened. This reaction was not noted in the other strains used in the experiment.

Autopsy records reveal that every strain A mouse developed multiple lung nodules, while of the 34 strain I mice which developed subcutaneous tumors 5 had from 1 to 3 pulmonary tumors and of the 4 strain I animals killed at the conclusion of the experiment, 3 each had a single pulmonary tumor. From these findings it may be concluded that the strain A mice are more susceptible than those of strain I to the development of induced lung growths. Pulmonary growths were also found in 3 of the Y mice which had developed subcutaneous sarcomas at the injection site and histological examination revealed these to be primary lung growths. The occurrence of lung tumors in mice of strain Y will be mentioned later in this report.

In this experiment the strain A mice developed ulceration at the site of injection, but they are included in the results since subcutaneous tumors arose and the presence of lung tumors within 10 weeks after subcutaneous injection is regarded as being of interest. In this laboratory efforts to ascertain the response of mice to lard solutions of carcinogenic agents are not considered satisfactory when ulceration occurs at the injection site. During the course of several experiments in which mice had been injected subcutaneously with lard solutions of 1:2:5:6-dibenzanthracene or methylcholanthrene, the animals which received the methylcholanthrene developed ulcerations, and induced tumors appeared earlier in the dibenzanthracene-injected mice. When the experiments were repeated with smaller amounts of the hydrocarbons and none of the mice developed ulceration, it was found that induced tumors arose earlier in the methylcholanthrene-injected mice. In view of this it was concluded that an amount of a hydrocarbon so great as to produce ulceration should not be used in efforts to ascertain its carcinogenic activity, for in all probability the lard solution escapes through the injured skin.

It has been noted that of all strains of mice which have been injected subcutaneously with lard solutions of carcinogenic hydrocarbons strain A mice have thus far proved to be the most susceptible to ulceration. Strain I animals are also rather susceptible while strain C_3H mice are the most resistant. The strain A mice used in this

experiment are the only ones mentioned in this report which had ulcerations at the site of injection.

EXPERIMENT 4

Mice of strains C_3H and Y, all of which were 3 months of age, were given methylcholanthrene-cholesterol pellets subcutaneously in the right axillary region. The pellets were prepared according to Shear's (*29*) technique and contained 5 percent of methylcholanthrene. Each pellet weighed approximately 10 mg; thus, each mouse received about 0.5 mg of methylcholanthrene dissolved in 9.5 mg of cholesterol. The experiment was performed to see whether the medium in which the hydrocarbon was dissolved could be responsible for the difference in susceptibility revealed by the injection of lard solutions. The pellets were inserted on September 21, 1937, and the first definite tumor was noted in a C_3H mouse on November 12, 1937. The experiment was conducted until March 17, 1938, when all surviving mice were killed. The results are summarized in table 5.

TABLE 5.—*Experiment 4: Time of appearance of tumors in strains C_3H and Y mice following subcutaneous insertion of methylcholanthrene-cholesterol pellets*

Time in weeks			8	10	12	14	16	18	20	22	24			
Strain	Sex	Number of mice used	Number of tumors									Total number of tumors	Number dying without tumor	Number killed Mar. 17, 1938
C_3H	F	25	1	1	5	7	3	4	----	1	----	22	1	2
C_3H	M	20	----	1	2	8	1	6	----	----	1	19	1	0
Y	F	19	----	----	----	----	----	----	----	2	2	4	1	14
Y	M	12	----	----	----	1	----	----	----	----	1	2	1	9

The conclusion to be drawn from the figures presented in table 5 is that methylcholanthrene pellets induced tumors in strain C_3H mice earlier than in the strain Y mice. This suggests that the medium in which the cancer-inducing compound was dissolved had little influence upon its relative carcinogenicity for the two strains.

DISCUSSION

It is believed that the results of earlier investigations and those presented herein, together with a number of unpublished experiments, furnish sufficient information to list the various strains of mice according to their susceptibility to subcutaneous and pulmonary tumors induced by certain hydrocarbons. An effort to summarize the findings as regards the eight strains has been made and is presented in table 6.

In the first column of table 6 the strains are listed in order of their susceptibility to subcutaneous tumors induced by lard solutions of

1:2:5:6-dibenzanthracene or methylcholanthrene. Strain C_3H is considerably more susceptible than the other strains, as revealed by a number of experiments, and it is of interest that the strain shows a remarkable uniformity in its reaction to lard solutions of the hydrocarbons, for in the majority of experiments performed thus far 0.8 mg of 1:2:5:6-dibenzanthracene has induced tumors in these mice in the average time of 17 to 18 weeks. This uniformity in reaction to the carcinogenic agent may be due to the high degree of susceptibility of the C_3H mice, for it is possible that even 0.8 mg may overcome less pronounced variations in individual resistance. In fact, experiments performed in collaboration with Dr. M. J. Shear have revealed that so far as C_3H mice are concerned there is no pronounced difference in the latent period when they are injected subcutaneously with 1 or 2 mg of methylcholanthrene. Strains I and Y are both more resistant to the hydrocarbons than the other 6 strains. A report dealing with the pronounced resistance of Y mice when compared with C_3H animals has been published previously (*11*), and the experiments recorded in this paper place the I mice close to those of strain Y in natural resistance to the two hydrocarbons.

TABLE 6.—*Summary of 8 highly inbred strains of mice showing susceptibility to spontaneous, mammary, and pulmonary tumors, induced subcutaneous and pulmonary tumors, and natural resistance to transplantable tumors*

Strains listed in order of susceptibility to subcutaneous tumors induced by carcinogenic hydrocarbons	Incidence of spontaneous mammary tumors in breeding females	Incidence of spontaneous pulmonary tumors	Susceptibility to pulmonary tumors induced by subcutaneous injection of lard-dibenzanthracene solutions	Natural resistance to cutaneous growth of sarcoma 37	Natural resistance to cutaneous growth of sarcoma 180	Remarks
C_3H	95 to 100 percent	(?)	Medium	High	Low	Develop spontaneous and induced hepatomas.
C	Less than 5 percent	20 to 30 percent.	High	Low	do	An incidence of 50 percent of spontaneous lymphocytomas.
M	"Medium to low"	Low	Low	High	do	
C57 black	Less than 1 percent	do	do	do	do	Very low incidence of spontaneous mammary tumors.
A	80 to 85 percent	80 to 85 percent.	Very high	do	do	Excellent test animals for study of spontaneous or induced pulmonary tumors. Susceptible to ulceration when injected subcutaneously.
D	65 to 100 percent	Low	Low	Low	do	Good soil for propagation of well known transplantable mouse tumors.
I	Less than 5 percent	(?)	Medium	High	High	Develop spontaneous hyperplasia of the epithelium in the pyloric portion of stomach. Resistant to growth of sarcoma 180.
Y	"Medium"	(?)	Medium to low.	Low	Low	Very resistant to induction of sarcoma by hydrocarbons but very susceptible to the growth of transplantable sarcomas.

The remaining five strains are regarded as a group of intermediate susceptibility, since they do not exhibit any pronounced differences. It is believed, however, that strain C is the most susceptible and strain D the most resistant of this group. There is little difference between the susceptibilities of strains M and C57 black, but the M mice may be the more susceptible. Mice of strain A are placed lower than those of strains C, M, and C57 black, although they may be just as susceptible; but the predisposition of these animals to develop ulceration at the injection site makes it difficult to determine their exact status. Strain D is placed last in the intermediate group chiefly on the basis of unpublished experiments performed in this laboratory.

It is desirable to emphasize that the listing is on the basis of susceptibility to subcutaneous injections of lard solutions, for it is possible that the strains may reveal a different order of resistance when subjected to skin painting. It is worthy of note that Korteweg (*21*) found mice of strain D to be more resistant than those of strain C57 black to tar-induced skin tumors, and Branch (*17*) found strain C57 black mice more susceptible than those of strain A when subjected to skin painting with 1:2:5:6-dibenzanthracene dissolved in benzol. It should be recorded that the listing of the strains in the first column of table 6 is based upon the results obtained with lard solutions of one lot of 1:2:5:6-dibenzanthracene. Indeed, in all the experiments published from this laboratory in which mice were injected with a lard-dibenzanthracene solution, this one lot of the compound, purchased from the Eastman Kodak Co., has been used. The material is not pure, as revealed by its yellow color.

The resistance of a strain is determined by the period of time elapsing between injection and the appearance of tumor. This period is referred to as the latent period. There are a number of factors affecting the latent period in mice, among which are the cancer-inducing power and amount of the carcinogen used, as well as the condition in which the substance is injected; for it has been shown (*5*) that, when injected subcutaneously into C_3H mice, a lard solution of 1:2:5:6-dibenzanthracene induced tumors earlier than did colloidal suspensions or the crystalline material. Hence, it is important to employ a uniform amount of a cancer-producing compound dissolved or suspended in equal quantities of a given medium when comparing the susceptibility of different animals. The wide variations in susceptibility revealed by the strains of mice mentioned in this paper indicate the necessity of using inbred animals when comparing the carcinogenic activity of different substances. Strain C_3H mice should serve as excellent test animals in this respect so far as the cancer-inciting hydrocarbons are concerned; for their high degree of sus-

ceptibility, together with their resistance to ulceration, should enable one to detect weakly carcinogenic compounds, while the use of strains I and Y mice in similar tests may fail to disclose the carcinogenic activity of such compounds.

It is obvious from the results of experiment 3 that a large amount of a carcinogenic hydrocarbon will produce tumors in all strains of mice regardless of their genetic constitutions, and it is possible that much larger amounts may wipe out any strain differences in resistance; but the use of such large quantities is usually accompanied by ulceration which is detrimental to the accurate determination of carcinogenic activity.

In the second column of table 6 is shown the incidence of spontaneous mammary gland tumors in breeding females of the various strains. Strains C_3H, A, and D have a high incidence (from 65 to 100 percent), while strains C57 black, C, and I have a low incidence (from 1 to 5 percent) of such growths. Information concerning strains M and Y is presented in the table as obtained from the Bar Harbor List of Stocks. There are no published accounts of strain I in this respect, but experience with the strain in this laboratory indicates that the incidence of breast tumors is low. It is obvious that there is no correlation between the incidence of spontaneous mammary tumors and susceptibility to the induction of subcutaneous tumors by injections of lard solutions of either hydrocarbon.

In the third column of the table is shown the incidence of spontaneous pulmonary tumors in the strains according to investigations published up to the present time. Strain A mice are by far the most susceptible in this respect with strain C mice next in order. Animals of strains I, C_3H, and Y show definite evidence of susceptibility, and they are listed as questionable in the table because precise information regarding the incidence of spontaneous pulmonary tumors in them is as yet unknown. The remaining 3 strains, M, C57 black, and D, all show a low incidence (less than 5 percent) of spontaneous lung growths.

The susceptibility of the various strains to pulmonary tumors induced by subcutaneous injection of 1:2:5:6-dibenzanthracene is listed in the fourth column of table 6. There is little doubt that strain A mice are the most susceptible to these induced tumors. Investigations dealing with this strain and the appearance of induced lung tumors have been reported from this laboratory (*3, 4, 7, 9, 11*), in which it was shown that the lungs of these mice are more susceptible to the carcinogenic activity of 1:2:5:6-dibenzanthracene than are their subcutaneous tissues. Mice of strains C57 black, M, and D are very resistant to induced lung tumors, especially those of strain C57 black.

Considerable difficulty is encountered in designating the remaining strains in a manner which will be clear to the reader. It is not only the number of mice which develop tumors which determines susceptibility, but the number of tumors produced in individual mice of various strains, as well as the latent period, must also be taken into account. Because of the pronounced susceptibility of the strain A mice in all these respects they are listed as "very high," while the strain C mice, which are next to the A mice in susceptibility, are listed as "high." Other strains which exhibit definite susceptibility are all listed as "medium." After taking into account the various factors just mentioned, the strains listed as "medium" in the table may be arranged in order of susceptibility as follows: Strains I, C_3H, and Y.

The occurrence of a few lung growths in strain Y mice following subcutaneous injection of 1:2:5:6-dibenzanthracene raises an interesting question, since the pronounced resistance of their subcutaneous tissues results in tumors appearing after a long latent period and gives the agent a longer period of time to act directly or indirectly upon the lung tissues. Would the C57 black animals also develop a few induced pulmonary growths if their subcutaneous tissues were as resistant as those of strain Y mice? A response to this question is suggested when mice of strains A and C_3H are used as experimental animals. If both strains are injected subcutaneously with 0.8 mg of 1:2:5:6-dibenzanthracene dissolved in 0.2 cc of lard, the C_3H animals develop sarcomas at the site of injection and die before tumors are found in their lungs, while strain A mice develop primary pulmonary growths before sarcomas appear at the injection site. Indeed, special techniques must be employed (*5*) to demonstrate the susceptibility of C_3H mice to induced pulmonary growths. Such results are due to wide variations in susceptibility on the part of different tissues and suggest that intravenous injection should be used for precise determinations of lung tumor susceptibility.

The appearance of primary lung tumors in mice of strains C, C_3H, I, and Y following the injection of a carcinogenic hydrocarbon presents an opportunity to ascertain whether such growths are induced more readily in strains which have a tendency to develop them spontaneously. Strain A mice are known to possess a special organ susceptibility to the development of spontaneous pulmonary growths, and the high incidence of induced tumors in these mice implies that these growths can be evoked with greater ease in animals which develop them spontaneously. Accordingly, efforts have been made to ascertain whether mice of strains C, C_3H, I, and Y also have a higher incidence of spontaneous lung growths than those strains which failed to develop induced pulmonary tumors, and thus far the results of these efforts tend to support this view. It has been noted in the Bar Harbor Laboratories that strain C mice have a tendency

toward the development of spontaneous lung tumors, and this finding has been confirmed in this laboratory. Up to the present time approximately 30 percent of normal untreated strain C mice which came to autopsy when one year of age or older have had primary tumors within their lungs. As just noted, the strain C animals rank next to those of strain A in susceptibility to induced lung tumors, and the same relationship exists for the occurrence of spontaneous lung growths in the colonies bred in this laboratory. In dealing with the occurrence of spontaneous pulmonary tumors in strain C_3H mice in a previous report (*5*), it was stated that up to that time the experience of this and other laboratories indicated a very low incidence of such tumors. The occurrence of breast cancer in virtually all breeding females at an average age of 8 to 9 months has made it difficult to accumulate any information from female mice, and males have been used extensively for experimental purposes. However, of 13 female mice which were free from breast tumor and came to autopsy when 19 to 24 months of age, 4 had spontaneous pulmonary tumors, which indicates that these mice have a tendency to develop pulmonary tumors late in life.

So far as the occurrence of spontaneous lung growths in old mice of strains I and Y are concerned, there has been a relatively small number autopsied up to the present time, but these have furnished some significant evidence. The I mice develop hyperplasia of the epithelium lining the pyloric portion of the stomach, which causes death at an early age; but spontaneous lung growths have been found in some of these animals. Similar growths have been found in older mice of strain Y. The numbers of mice of strains C_3H, I, and Y which have come to autopsy are too small to be of statistical value in determining the incidence of spontaneous lung tumors in the strains, but sufficient numbers have been examined to state with certainty that such tumors are not uncommon in old mice of all 3 strains. Further studies concerning the incidence of tumors other than mammary tumors in these 3 strains are now in progress.

From the study of induced tumors in the lungs of the 8 strains of mice it may be concluded that the strains exhibit striking variations in susceptibility to these growths, and those strains which develop the most spontaneous pulmonary tumors are the most susceptible to the induced growths. Since the induction of subcutaneous tumors in all the strains is possible regardless of their genetic constitution, it is possible that the differences in susceptibility of the various strains to induced pulmonary tumors may also be a matter of degree only. Here, again, the study tends to emphasize the importance of the use of certain strains as test animals for the induction of lung tumors by carcinogenic hydrocarbons.

In the fifth and sixth columns of table 6 the strains are listed according to their natural resistance to cutaneous growth of two well known transplantable mouse sarcomas, namely, sarcoma 37 and sarcoma 180. The details of these investigations have been presented in an earlier report (*5*), in which it was recorded that in practically every mouse of 5 strains the cutaneous growth of sarcoma 37 regressed spontaneously, while in 3 other strains the tumor grew progressively and killed the animals. Sarcoma 180 grew progressively in 7 of the strains and caused death, but in one strain (strain I) most of the cutaneous growths receded. In the table those strains which possessed sufficient natural resistance to overcome the growth of cutaneous tumors are designated as "high," while those in which the tumors grew progressively are designated as "low." It is seen that there is no correlation between the natural resistance of the strains to the growth of sarcoma 37 and their incidence of spontaneous mammary tumors or their susceptibility to induced tumors.

The last column of table 6 contains pertinent remarks concerning the strains of mice which may be of interest to workers in the field of experimental cancer. These characteristics of the strains will be discussed in the following summary of the outstanding features exhibited by each strain.

Strain C_3H.—Of the strains used in this laboratory, these mice have thus far proved to be the most susceptible to subcutaneous tumors induced by the carcinogenic hydrocarbons. Their lungs are also susceptible to the induction of tumors by the hydrocarbons. The breeding and the nonbreeding females are the most susceptible to the development of spontaneous mammary tumors, both showing an incidence of from 95 to 100 percent. They are resistant to cutaneous growth of sarcoma 37 but succumb to cutaneous growth of sarcoma 180. It has been found that these mice are similar to the strain CBA mice of Strong (*33*) in that they develop benign hepatomas late in life. In an earlier paper (*5*) the occurrence of hepatomas in these mice following the subcutaneous injection of 1:2:5:6-dibenzanthracene was discussed. As in the case of the lung tumors, which have been mentioned previously in this paper, the presence of spontaneous liver growths in these animals had not been noted in this and other laboratories where the strain is under observation. Since that time hepatomas have been found in older mice of this strain which were raised in this laboratory; and of the 13 female mice mentioned previously in this report, which ranged in age from 19 to 24 months, 4 had this type of growth within or attached to their livers. The finding of spontaneous lung and liver tumors in strain C_3H mice is of special interest, for in the previous report (*5*) it was suggested that such growths may occur spontaneously in old

C_3H animals. The occurrence of spontaneous and induced hepatomas in these mice will be discussed further in a future report.

Strain C.—These mice are of medium susceptibility to the induction of subcutaneous and lung tumors by the hydrocarbons. They show an incidence of about 30 percent spontaneous pulmonary growths, and the breeding females have a low incidence of spontaneous mammary tumors. They succumb to cutaneous growth of both sarcoma 37 and sarcoma 180. It has also been noted that many of the mice develop lymphocytomas after subcutaneous injection of 1:2:5:6-dibenzanthracene or methylcholanthrene. Inasmuch as the mice also develop lymphocytomas spontaneously, investigations are now in progress to determine whether the carcinogens hasten the appearance of this type of tumor.

Strain M.—This strain is in the intermediate group in respect to susceptibility to induced subcutaneous tumors and is resistant to induced lung tumors. The incidence of spontaneous mammary and lung tumors is low. Cutaneous growths of sarcoma 37 regress spontaneously in practically all the mice, but sarcoma 180 grows progressively.

Strain C57 black.—This strain is related to strain M, just mentioned, and is similar to it in the degree of susceptibility to induced subcutaneous and pulmonary tumors as well as natural resistance to cutaneous growths of the two sarcomas. The strain is, perhaps, best known as one in which breeding females are very resistant to the development of spontaneous mammary cancer and in which very few develop spontaneous pulmonary tumors. As mentioned previously in this study, the response of these mice to the hydrocarbons suggests a sex difference in susceptibility to induced subcutaneous tumors.

Strain A.—These mice are of an intermediate degree of susceptibility to induced subcutaneous tumors. They have the highest incidence (about 85 percent) of spontaneous pulmonary growths of any strain described up to the present time, and the breeding females show a high incidence (80 to 85 percent) of spontaneous mammary tumors. Of all the strains included in this report this is the most susceptible to ulceration at the site of subcutaneous injection. The mice have proved to be excellent experimental animals when used in investigations which deal with pulmonary tumors in mice. Most of them overcome the growth of sarcoma 37 but succumb to the growth energy of sarcoma 180.

Strain D.—This strain is rather resistant to induced subcutaneous and lung tumors. The breeding females have a high incidence (65 to 100 percent) of spontaneous mammary tumors. All the mice die when inoculated in the skin with sarcoma 37 or sarcoma 180. Experience in this laboratory suggests that these mice are excellent soil for the propagation of well-known transplantable mouse tumors, and appear

to be incapable of developing any appreciable degree of immunity following the inoculation of these tumors.

Strain I.—These mice are very resistant to the development of induced subcutaneous tumors but are susceptible to the development of induced lung tumors. The incidence of spontaneous mammary tumors is low, but spontaneous pulmonary growths are known to occur in these mice. The strain exhibits a remarkable resistance to the transplantable sarcomas, and the ability of the mice to overcome the growth of sarcoma 180, which is a highly malignant tumor, is of special interest. The strain is susceptible to an adenomatous lesion of the stomach which has been described elsewhere (*10*).

Strain Y.—This strain is very resistant to induced subcutaneous tumors, and a few pulmonary growths have been found in injected mice. The breeding females have a relatively low incidence of spontaneous mammary tumors, and spontaneous lung growths have been found in some old mice of the strain. The strain is very susceptible to cutaneous growths of sarcoma 37 and sarcoma 180, which is rather interesting when compared with the high resistance of strain I mice in this respect. Both strains are resistant to the development of induced subcutaneous sarcomas, and strain I mice are also resistant to the transplantable sarcomas, while the mice of strain Y appear to be especially susceptible to the growth powers of the transplantable tumors.

SUMMARY AND CONCLUSIONS

Eight strains of highly inbred mice have been used in these investigations. In these strains the incidence of spontaneous mammary tumors in the breeding females varies from less than 5.0 percent to practically 100 percent, according to strain. Each strain has been tested for susceptibility to the induction of subcutaneous and pulmonary tumors by subcutaneous injection of lard solutions of carcinogenic hydrocarbons. Wide variations in susceptibility to both types of induced growths were encountered in the different strains. Those strains which develop pulmonary tumors spontaneously were found to be the most susceptible to induced lung tumors. The response of those strains which develop lung tumors spontaneously when injected with hydrocarbons may be compared with the response of high mammary tumor strains when subjected to treatment with estrin. There is no correlation between the susceptibility to spontaneous mammary tumors and susceptibility to the induction of subcutaneous growths.

The strains also vary in their susceptibility to the cutaneous growth of transplantable tumors; but, here again, there is no correlation between the susceptibility to spontaneous tumors and susceptibility to propagable growths.

It is believed that generalization should not be made from the results attending these studies. The induced tumors were evoked only by 1: 2: 5: 6-dibenzanthracene or methylcholanthrene, and the response of the strains to transplantable mouse tumors applies only to the growth of sarcoma 37 and sarcoma 180.

The studies yield information concerning the characteristics of the strains of mice which should be of assistance in the selection of a suitable strain for certain experimental purposes. Since in these strains there is no correlation between the susceptibility to the induction of subcutaneous tumors and the natural resistance to the growth of transplantable tumors or the development of spontaneous mammary tumors, the conclusion may be drawn from the investigations that, up to the present time, a strain of mice has not been found which is resistant or susceptible to all types of tumor growth.

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THE INCIDENCE OF INDUCED SUBCUTANEOUS AND PULMONARY TUMORS AND SPONTANEOUS MAMMARY TUMORS IN HYBRID MICE*

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In previous communications (*4, 7*) it was shown that mice of strains Y and I were far more resistant than those of strain C_3H to the carcinogenic power of 1:2:5:6-dibenzanthracene or methylcholanthrene when the hydrocarbons were dissolved in lard and injected subcutaneously. It appeared that a series of cross-breeding experiments between these strains of mice might be of interest. The purpose of this report is to record briefly the results of a preliminary experiment in which mice of strain C_3H were mated to mice of strains Y or I and the offspring injected subcutaneously with 1:2:5:6-dibenzanthracene. The report also includes observations on the influence exerted by

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hybridization on the occurrence of induced pulmonary tumors and on the occurrence of spontaneous mammary tumors.

EXPERIMENTAL PROCEDURE

Young adult mice of strains C_3H, Y, and I were mated on April 10, 1937, as follows: 16 females of strain C_3H to males of strain I; 11 females of strain I to males of strain C_3H; 12 females of strain C_3H to males of strain Y; and 9 females of strain Y to males of strain C_3H. The offspring were born between May 1 and June 1, 1937. The number and sex of the hybrid mice are summarized below:

	Females	Males	Total
Strain C_3H mother and strain I father	57	48	105
Strain I mother and strain C_3H father	23	32	55
Strain C_3H mother and strain Y father	28	44	72
Strain Y mother and strain C_3H father	14	24	38
Total	122	148	270

All the mice received individual numbers and so a complete record of ancestry and other pertinent data were available.

DIBENZANTHRACENE INJECTION

A sufficient quantity of a lard-dibenzanthracene solution was prepared at one time to inject all the experimental animals. Each cubic centimeter of lard contained 4 milligrams of 1:2:5:6-dibenzanthracene.

On June 30, 1937, all 48 females of the parent stocks and 206 (92 females and 114 males) of the hybrid mice each received 0.2 cc of the lard-dibenzanthracene solution in the subcutaneous tissues of the right axilla. The injected material contained 0.8 mg of 1:2:5:6-dibenzanthracene. Sixty-four (30 females and 34 males) of the hybrid mice were set aside as untreated normal controls.

THE OCCURRENCE OF INDUCED SUBCUTANEOUS TUMORS

Following the injection, the mice were examined at weekly intervals for the presence of induced tumors, and the first tumor was found in a C_3H mouse on September 8, 1937. As the mice developed induced tumors, they were killed and the internal organs were examined carefully for the presence of macroscopic growths. All surviving injected mice were killed on March 24, 1938.

The time of appearance of subcutaneous tumors in the female parent mice is summarized in table 1.

It is clear that the C_3H mice were considerably more susceptible than those of strains Y or I to the carcinogenic activity of the compound; results similar to those observed in other experiments (*4*, *7*) in

which mice of these strains were injected with the same carcinogenic hydrocarbon.

The time of appearance of subcutaneous tumors in the hybrid mice is shown in table 2.

TABLE 1.—*Time of appearance of induced tumors in the parent mice of strains C_3H, I, and Y following subcutaneous injection of 0.8 mg of 1:2:5:6-dibenzanthracene dissolved in 0.2 cc of lard*

Time in weeks...		10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	Total number of tumors	Average time, in weeks	Number that died without induced tumor	Number killed Mar. 24, 1938
Strain	Number of mice	Number of tumors																		
C_3H	28	2	1	3	7	3	4	1	1	---	---	---	---	---	---	---	22	16.1	6	0
I	11	---	---	---	---	---	---	---	---	---	2	---	3	2	---		7	32.7	1	3
Y	9	---	---	---	---	---	---	---	---	1	---	---	---	1	1		3	33.7	3	3

TABLE 2.—*Time of appearance of induced tumors in hybrid mice following subcutaneous injection of 0.8 mg of 1:2:5:6-dibenzanthracene dissolved in 0.2 cc of lard*

Time in weeks				12	14	16	18	20	22	24	26	28	30	32	34	36	38				
Mothers from strain	Fathers from strain	Sex	Number of mice	Number of tumors														Total number of tumors	Average time, in weeks	Number that died without induced tumor	Number killed Mar. 24, 1938
C_3H	I	F	45	---	---	1	2	6	6	4	4	3	6	1	3	1	---	37	25.0	6	2
C_3H	I	M	36	---	1	---	1	1	3	2	5	1	2	1	1	3	---	21	26.0	0	15
I	C_3H	F	17	---	---	2	---	---	3	2	1	2	2	---	---	---	---	12	23.4	0	5
I	C_3H	M	24	---	---	---	1	---	---	4	1	2	5	1	1	2	1	18	28.6	1	5
C_3H	Y	F	20	1	---	---	1	1	3	2	2	---	1	---	2	3	1	17	26.4	0	3
C_3H	Y	M	34	1	---	---	1	1	2	5	3	1	6	4	2	2	---	28	27.0	1	5
Y	C_3H	F	10	---	---	---	1	---	---	---	---	1	2	---	---	---	---	4	25.7	0	6
Y	C_3H	M	20	---	---	1	1	1	---	3	1	1	2	2	---	---	2	14	26.8	0	6

In table 2 it is seen that the hybrid animals, regardless of origin, were of intermediate susceptibility when compared with the parent strains, since they were, on the average, more resistant than the C_3H mice and more susceptible than the Y or I animals. It will be noted that of 36 male mice derived from C_3H females and I males 21, or 58 percent, developed tumors at the injection site during the period of time covered by the experiment; while of 45 female litter mates 37, or 81 percent, developed tumors. An analysis of the individual records of these mice has thus far failed to reveal any influence responsible for this variation in susceptibility.

So far as genetic influences are concerned, the results in the hybrid mice suggest that if susceptibility to the action of the carcinogen has a genetic basis it is probably due to the influence of multiple factors.

Of the female parent mice, 4 strain I, one strain C_3H, and one strain Y developed induced pulmonary tumors. The production of induced lung growths in these 3 strains of mice has been discussed in a previous report (*7*).

Referring to table 2 it can be seen that of 122 hybrid mice procured by reciprocal breeding between strains C_3H and I, 88 developed induced subcutaneous tumors, and of these latter mice 78, or 88 percent, also had induced pulmonary tumors. All of the 27 mice of this group, killed when the experiment was terminated on March 24, 1938, were free from tumor at the injection site but 24, or 88 percent, had induced lung tumors.

From the reciprocal matings of strains C_3H and I there were 38 mice (18 females and 20 males), set aside as untreated controls. Of these 38 mice, 12 females developed spontaneous breast tumors and died between November 30, 1937, and March 6, 1938. None had a pulmonary tumor. The remaining 26 mice were killed on May 23, 1938, when they were one year of age, and one had a pulmonary tumor. The absence of pulmonary tumors in these control mice shows that the pulmonary growths arising in the injected mice were induced.

Table 2 also reveals that of 84 hybrids resulting from reciprocal crossing of strains C_3H and Y, 63, or 75 percent, developed induced subcutaneous tumors. However, of these 63 mice, only 7, or 11 percent, had pulmonary growths. When the 20 mice of this group which were free from induced subcutaneous tumors were killed on March 24, 1938, it was found that 4, or 20 percent, had induced tumors within their lungs. There were 26 of these hybrids used as untreated controls; and when 18 were sacrificed on May 23, 1938, all were free from pulmonary tumors.

From this it may be concluded that the hybrid mice derived by mating C_3H and I mice were more susceptible to induced pulmonary tumors than those procured by mating C_3H and Y mice. Indeed, the hybridization of C_3H with I mice resulted in offspring which were more susceptible to induced lung growths than either of the parent strains. From the standpoint of genetics this outcome suggests the summation of similar factors within the parent strains.

Findings in previous investigations (*1*, *5*) in which hybrids were obtained by mating strain A and strain C57 black mice showed that the susceptibility of the lungs to tumor formation induced by the hydrocarbon was inherited in a dominant manner. The results of the experiment recorded herein are not in accord with the earlier findings; for if the susceptibility of the lungs of strain C_3H mice to induced tumors were inherited as a dominant factor, the lungs of

hybrids resulting from the mating of C_3H to either I or Y mice should have been equally susceptible.

The occasional occurrence of induced pulmonary tumors in hybrids derived from mating C_3H to Y mice revealed that the hybrids were not wholly resistant, indicating that, although genetic factors are involved, they may control the degree of susceptibility only.

THE OCCURRENCE OF SPONTANEOUS MAMMARY TUMORS

It has been recorded in earlier papers (*2*, *6*) that the breeding and nonbreeding females of strain C_3H have a high incidence of spontaneous mammary tumors while experience in this laboratory with both strain I and Y indicates that these strains are resistant to the same type of tumor.

Of the 28 strain C_3H mice used as parent mice in this investigation 6 developed spontaneous breast tumors and succumbed before the occurrence of an induced tumor at the site of injection. These mice are listed in table 1 as dying without induced tumor. One mouse developed both an induced sarcoma and spontaneous breast tumor. Thus, 7, or 25 percent, of the C_3H animals developed mammary tumors during the course of the investigation.

Of the 45 injected female hybrids derived from C_3H females and I males, 5 developed spontaneous breast tumors before tumors arose at the injection site. These 5 mice are included in table 2 among the 6 animals of this group designated as dying without induced tumors. Of the 37 mice in this group which developed induced tumors, 8 also had spontaneous breast tumors. Hence, of the 45 mice in this group, 13, or 28 percent, developed spontaneous mammary cancers at an average age of 8 months. Furthermore, there were 12 female mice derived from crossing C_3H females and I males used as normal controls, and all of these developed breast tumors at an average age of 8 months.

The average age at which breast tumors arose in the above-mentioned mice is of special interest, for female hybrids used in this experiment were virgin mice, and it has been found (*6*) that virgin females of the parent C_3H strain develop breast tumors at an average age of 11.5 months. The results obtained with these hybrids suggest that, as in the case of induced pulmonary tumors, hybridization between the C_3H and I mice increases the susceptibility of the offspring to spontaneous breast tumors.[1] It is essential to record that Bittner (*8*) also mated C_3H females to I males and found that breast tumors appeared in the female progeny at an average age of 10.4 months, which compared favorably with the average tumor age of 10.7 months he reported for his colony of C_3H mice.

[1] In a previous communication (*3*) the occurrence of a stomach lesion in practically all strain I mice 8 months of age or older was reported. A similar lesion was not seen in any of the hybrids of this experiment suggesting a recessive factor if the lesion has a genetic basis.

Of the 17 injected female hybrids procured by mating I females and C_3H males none developed breast tumor. The occurrence of breast tumors in mice born to C_3H mothers and I fathers and the nonoccurrence of the same type of growth in mice born to I mothers and C_3H fathers supports the extra-chromosomal theory of the origin of spontaneous mammary cancer in mice.

Turning to the 20 injected female hybrids resulting from mating C_3H females to Y males and the 10 injected female hybrids born to Y mothers and C_3H fathers it was found that none developed spontaneous breast cancer. In addition there were 8 female mice derived by mating C_3H females and Y males which were used as normal controls. These mice were 13 months of age on June 15, 1938, and none has developed a breast tumor. Thus, it is seen that of 28 females born to C_3H mothers and Y fathers none developed a breast tumor while, as recorded in the preceding paragraphs, of 57 females born to C_3H mothers and I fathers, 25, or 43 percent, developed this type of growth.

The reason for the difference in susceptibility of the hybrids born to C_3H mothers remains obscure. Investigations (*11*) suggest that when highly inbred strains of mice are crossed the maternal influence plays an important part in the occurrence of breast tumors in the offspring, and recent evidence (*9*, *10*) has been presented which indicates that the agent or agents responsible for breast cancer in mice is present in the mother's milk. As stated previously, the outcome of this investigation shows that female mice born to C_3H mothers and I fathers were more susceptible to breast cancer than offspring born to C_3H females and their male litter mates, while females born to C_3H mothers and Y fathers were more resistant to breast tumors than the offspring of C_3H females and their male litter mates. Such evidence suggests that genetic factors may also be involved in the occurrence of breast cancer in mice.

The observation that hybridization increases the susceptibility of mice may be compared with the work of Gordon (*12*), who recorded that by the proper selection of non-tumorous parents, hybrid fish were obtained which developed melanosis. The problem is receiving further consideration.

SUMMARY

Reciprocal breeding was carried on between mice of strains C_3H and I and strains C_3H and Y. The female parent mice and most of the hybrid mice were injected subcutaneously with a lard-dibenzanthracene solution. The results of the investigation may be summarized as follows:

(1) The C_3H female parents were more susceptible to the carcinogen than either the I or Y female parents.

(2) The hybrid mice were of intermediate susceptibility when compared with the susceptibility of the parent strains.

(3) Hybrid mice derived by mating strain C_3H to strain I were considerably more susceptible to induced pulmonary tumors than those derived by mating strain C_3H to strain Y.

(4) Female hybrids born to C_3H mothers and I fathers were more susceptible to spontaneous mammary cancer than female hybrids born to C_3H mothers and Y fathers.

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DEATHS DURING WEEK ENDED AUGUST 27, 1938

[From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Aug. 27, 1938	Corresponding week, 1937
Data from 88 large cities of the United States:		
Total deaths	7,120	[1] 7,140
Average for 3 prior years	[1] 7,289	
Total deaths, first 34 weeks of year	280,563	304,052
Deaths under 1 year of age	560	[1] 511
Average for 3 prior years	[1] 505	
Deaths under 1 year of age, first 34 weeks of year	18,090	19,529
Data from industrial insurance companies:		
Policies in force	68,411,272	69,724,311
Number of death claims	11,019	10,801
Death claims per 1,000 policies in force, annual rate	8.4	8.1
Death claims per 1,000 policies, first 34 weeks of year, annual rate	9.3	10.2

[1] Data for 86 cities.

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers.

In these and the following tables, a zero (0) indicates a positive report and has the same significance as any other figure, while leaders (----) represent no report, with the implication that cases or deaths may have occurred but were not reported to the State health officer.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept 3, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median

Division and State	Diphtheria				Influenza				Measles			
	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median
NEW ENG.												
Maine	6	1	1	0	----	----	----	----	152	25	2	3
New Hampshire	0	0	1	0	----	----	----	----	10	1	----	----
Vermont	0	0	0	0	----	----	----	----	----	----	----	----
Massachusetts	1	1	3	4	----	----	----	----	22	19	14	21
Rhode Island	0	0	0	0	----	----	----	----	15	2	1	1
Connecticut	3	1	3	1	----	----	1	1	12	4	1	5
MID. ATL.												
New York	3	8	11	14	[1]1	[1]1	----	[1]2	30	75	78	75
New Jersey	0	0	2	4	10	8	----	2	16	13	20	16
Pennsylvania	8	16	12	19	----	----	----	----	71	138	131	83
E. NO. CEN.												
Ohio	13	17	8	17	----	----	----	19	10	13	38	27
Indiana [2]	5	3	4	9	5	3	14	14	5	3	13	3
Illinois [2]	9	13	15	16	6	9	6	4	7	11	44	15
Michigan	6	6	9	9	----	----	3	----	30	28	27	19
Wisconsin	4	2	2	2	27	15	10	16	84	47	33	33
W. NO. CEN.												
Minnesota	18	9	1	2	4	2	1	1	39	20	6	4
Iowa	16	8	2	5	6	3	----	----	8	4	1	1
Missouri	9	7	8	18	18	14	83	14	3	2	10	10
North Dakota	15	2	1	3	52	7	----	----	185	25	2	2
South Dakota	8	1	0	1	8	1	----	----	----	----	----	----
Nebraska	4	1	1	2	----	----	----	----	8	2	2	2
Kansas	3	1	2	5	----	----	----	----	8	3	2	5

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 3, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Diphtheria				Influenza				Measles			
	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median
SO. ATL.												
Delaware	40	2	0	1								1
Maryland [2 3 4]	19	6	6	3	9	3	2	2	3	1	6	6
Dist. of Col	17	2	5	5					8	1	4	1
Virginia [2]	69	36	23	24					6	3	13	13
West Virginia	22	8	11	11	48	17	16	16	3	1	9	10
North Carolina [3]	91	61	44	36	1	1		4	30	20	24	11
South Carolina [4]	64	23	3	4	286	103	50	53	3	1	10	6
Georgia [4]	57	34	14	14								
Florida [4]	19	6	12	12					69	22		1
E. SO. CEN.												
Kentucky	36	29	19	19	5	3	1	1			18	9
Tennessee	9	5	6	17	23	13	6	6	4	2	31	3
Alabama [4]	72	40	13	26	23	13	5	4			3	13
Mississippi [3]	59	23	7	18								
W. SO. CEN.												
Arkansas	36	14	14	12	38	15	4	3	33	13	3	
Louisiana	17	7	7	17	7	3	7	8				
Oklahoma	16	8	4	6	25	12	17	7	16	8		
Texas [4]	26	31	36	37	57	67	76	27	12	14	8	18
MOUNTAIN												
Montana	19	2	1	1					97	10	7	4
Idaho	0	0	1	0	11	1			53	5		1
Wyoming	0	0	0	0					89	4		1
Colorado	97	20	2	3					34	7	13	6
New Mexico	62	5	2	2					12	1	5	1
Arizona	0	0	0	2	165	13	7	6	51	4		1
Utah [3]	0	0	5	0			5		80	8	12	3
PACIFIC												
Washington	0	0	0	0					13	4	21	5
Oregon	25	5	0	1	20	4	14	5	25	5	4	5
California [3]	13	15	14	24	10	12	11	10	69	81	17	43
Total	19	470	335	463	17	343	339	314	27	650	633	609
35 weeks	18	15,410	14,417	19,098	67	46,816	275,124	142,093	893	761,975	242,553	342,857

Division and State	Meningitis, meningococcus				Poliomyelitis				Scarlet fever			
	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median
NEW ENG.												
Maine	0	0	0	0	0	0	19	3	12	2	4	7
New Hampshire	0	0	0	0	0	0	4	0	0	0	0	1
Vermont	0	0	0	0	0	0	0	0	14	1	1	1
Massachusetts	0	0	0	1	1.2	1	44	32	33	28	12	31
Rhode Island	0	0	0	0	0	0	3	1	0	0	3	6
Connecticut	0	0	0	0	6	2	10	10	18	6	4	4
MID. ATL.												
New York	0.8	2	3	3	6	14	52	52	16	40	72	72
New Jersey	0	0	1	1	4	3	10	10	11	9	13	16
Pennsylvania	2	4	4	14	1.5	3	19	13	38	74	66	66

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 3, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Meningitis, meningococcus				Poliomyelitis				Scarlet fever			
	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median
E. NO. CEN.												
Ohio	0.8	1	1	1	1.5	2	31	22	26	34	28	69
Indiana [3]	1.5	1	1	1	0	0	11	2	56	37	28	22
Illinois [3]	0	0	3	3	2	3	106	19	36	55	77	83
Michigan	0	0	0	1	5	5	34	26	67	62	96	51
Wisconsin	0	0	2	1	12	7	23	4	75	42	37	37
W. NO. CEN.												
Minnesota	0	0	1	0	2	1	18	8	41	21	14	18
Iowa	2	1	1	0	2	1	16	3	35	17	13	11
Missouri	0	0	1	2	0	0	25	1	21	16	24	19
North Dakota	0	0	0	0	0	0	3	2	66	9	4	4
South Dakota	0	0	1	0	0	0	5	1	45	6	6	6
Nebraska	0	0	0	0	0	0	19	0	15	4	5	2
Kansas	0	0	1	1	0	0	14	4	154	55	23	17
SO. ATL.												
Delaware	0	0	0	0	0	0	0	0	100	5	0	3
Maryland [2 3 4]	3	1	0	1	0	0	6	2	6	2	11	14
Dist. of Col	0	0	1	1	8	1	4	1	91	11	2	2
Virginia [3]	1.9	1	2	2	6	3	1	5	19	10	6	22
West Virginia	2.8	1	0	1	2.8	1	4	3	45	16	31	31
North Carolina [3]	4	3	2	2	3	2	8	3	36	24	22	25
South Carolina [4]	0	0	0	0	0	0	0	1	11	4	2	2
Georgia [4]	0	0	0	0	0	0	2	1	25	15	9	6
Florida [4]	0	0	1	0	3	1	2	0	6	2	0	2
E. SO. CEN.												
Kentucky	1.8	1	4	2	0	0	8	7	68	38	29	29
Tennessee	0	0	0	0	1.8	1	2	2	20	11	10	11
Alabama [4]	7	4	1	0	4	2	5	4	31	17	10	11
Mississippi [3]	2.6	1	0	0	5	2	10	0	21	8	5	8
W. SO. CEN.												
Arkansas	0	0	1	0	0	0	6	0	10	4	10	7
Louisiana	2.4	1	1	1	0	0	4	1	20	8	5	10
Oklahoma	0	0	2	0	0	0	9	0	10	5	14	6
Texas [4]	1.7	2	2	0	0.8	1	36	3	29	34	24	21
MOUNTAIN												
Montana	10	1	0	0	19	2	3	0	77	8	10	5
Idaho	0	0	0	0	0	0	1	0	63	6	4	1
Wyoming	0	0	0	0	0	0	0	0	67	3	7	6
Colorado	0	0	0	0	0	0	20	2	34	7	15	11
New Mexico	0	0	1	0	0	0	0	0	25	2	0	2
Arizona	0	0	0	0	0	0	1	1	0	0	0	1
Utah [3]	0	0	0	0	0	0	2	0	70	7	47	10
PACIFIC												
Washington	3	1	1	0	3	1	1	2	25	8	14	12
Oregon	0	0	0	0	5	1	2	1	86	17	5	11
California [3]	0	0	3	3	2.5	3	38	24	45	53	56	54
Total	1	26	42	42	2.5	63	641	401	34	843	878	878
35 weeks	2.6	2,214	4,292	4,292	1.3	1,091	4,695	4,687	160	138,694	166,580	166,580

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 3, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued.

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough	
	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases
NEW ENG.										
Maine	0	0	0	0	6	1	1	3	146	24
New Hampshire	0	0	0	0	0	0	0	0	0	0
Vermont	0	0	0	0	0	0	0	0	259	19
Massachusetts	0	0	0	0	1	1	4	4	92	78
Rhode Island	0	0	0	0	8	1	0	0	77	10
Connecticut	0	0	0	0	9	3	3	4	84	28
MID. ATL.										
New York	0	0	0	0	11	28	28	31	195	484
New Jersey	0	0	0	0	18	15	5	6	223	186
Pennsylvania	0	0	0	0	12	24	39	25	163	319
E. NO. CEN.										
Ohio	0	0	0	0	22	29	43	43	115	149
Indiana [2]	5	3	0	0	24	16	8	16	12	8
Illinois [2]	1	2	1	1	13	20	22	28	334	504
Michigan	1	1	0	0	15	14	17	17	320	296
Wisconsin	0	0	1	1	9	5	3	1	716	402
W. NO. CEN.										
Minnesota	8	4	2	0	0	0	0	3	79	40
Iowa	0	0	4	0	8	4	5	5	53	26
Missouri	3	2	1	0	33	25	36	27	10	8
North Dakota	22	3	1	0	0	0	3	1	443	60
South Dakota	0	0	3	0	8	1	2	2	23	3
Nebraska	0	0	0	0	0	0	1	0	4	1
Kansas	3	1	0	1	31	11	5	14	104	37
SO. ATL.										
Delaware	0	0	0	0	40	2	0	1	160	8
Maryland [2 3 4]	0	0	0	0	31	10	17	17	71	23
Dist. of Col	0	0	0	0	58	7	5	1	133	16
Virginia [2]	0	0	0	0	13	7	19	36	17	9
West Virginia	0	0	0	0	109	39	17	18	112	40
North Carolina [2]	0	0	0	0	21	14	16	19	334	224
South Carolina [4]	0	0	0	0	53	19	10	18	192	69
Georgia [4]	0	0	0	0	30	18	16	38	27	16
Florida [4]	0	0	0	0	19	6	4	2	0	0
E. SO. CEN.										
Kentucky	0	0	0	0	39	22	34	52	52	29
Tennessee	0	0	0	0	16	9	13	35	16	9
Alabama [4]	2	1	2	0	29	16	12	18	11	6
Mississippi [3]	0	0	0	0	21	8	11	10	-------	-------
W. SO. CEN.										
Arkansas	0	0	0	0	76	30	13	12	43	17
Louisiana	0	0	0	0	32	13	19	19	54	22
Oklahoma	0	0	0	0	33	16	18	18	2	1
Texas [4]	0	0	1	1	43	51	65	43	95	112
MOUNTAIN										
Montana	0	0	11	1	0	0	2	5	551	57
Idaho	0	0	0	0	21	2	0	2	32	3
Wyoming	0	0	0	0	22	1	1	1	22	1
Colorado	0	0	2	1	54	11	4	6	151	31
New Mexico	74	6	0	0	124	10	5	13	371	30
Arizona	0	0	0	0	101	8	3	4	177	14
Utah [3]	0	0	0	0	20	2	1	2	281	28

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended Sept. 3, 1938, rates per 100,000 population (annual basis), and comparison with corresponding week of 1937 and 5-year median—Continued

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough	
	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases	Sept. 4, 1937, cases	1933–37 median	Sept. 3, 1938, rate	Sept. 3, 1938, cases
PACIFIC										
Washington	13	4	3	3	31	10	1	3	25	23
Oregon	61	12	1	0	10	2	8	7	41	8
California [1]	3	3	1	1	10	12	17	11	125	147
Total	2	42	34	23	22	543	556	703	149	3,625
35 weeks	15	12,769	8,080	5,368	11	9,273	9,374	10,718	178	151,689

[1] New York City only.
[2] Rocky Mountain spotted fever, week ended Sept. 3, 1938, 11 cases as follows: Indiana, 3; Illinois, 1; Maryland, 3; Virginia, 2; North Carolina, 1; California, 1.
[3] Week ended earlier than Saturday.
[4] Typhus fever, week ended Sept. 3, 1938, 60 cases as follows: Maryland, 1; South Carolina, 7; Georgia, 21; Florida, 2; Alabama, 13; Texas, 16.

SUMMARY OF MONTHLY REPORTS FROM STATES

The following summary of cases reported monthly by States is published weekly and covers only those States from which reports are received during the current week:

State	Meningitis, meningococcus	Diphtheria	Influenza	Malaria	Measles	Pellagra	Poliomyelitis	Scarlet fever	Small pox	Typhoid fever
July 1938										
North Dakota	2	11	25	----	159	----	1	37	26	1
Puerto Rico	0	35	14	2,380	12	1	1	0	0	66
Vermont	0	0	----	----	124	----	2	20	0	2
Virginia	8	57	177	26	440	24	12	47	0	110
Wisconsin	3	14	63	----	1,470	----	----	211	6	9

July 1938

	Cases
Chickenpox:	
North Dakota	45
Puerto Rico	10
Vermont	77
Virginia	31
Wisconsin	409
Dysentery:	
Puerto Rico	3
Virginia (diarrhea included)	1,200
Encephalitis, epidemic or lethargic:	
North Dakota	2
Filariasis:	
Puerto Rico	1
German measles:	
North Dakota	10
Mumps:	
North Dakota	25
Vermont	62
Virginia	77
Wisconsin	323
Paratyphoid fever:	
Virginia	1
Puerperal septicemia:	
Puerto Rico	1
Rocky Mountain spotted fever:	
Virginia	33
Septic sore throat:	
Virginia	28
Wisconsin	25
Tetanus:	
Puerto Rico	7
Tetanus, infantile:	
Puerto Rico	1
Trachoma:	
North Dakota	9
Virginia	1
Tularaemia:	
Virginia	10
Wisconsin	3
Undulant fever:	
North Dakota	1
Vermont	5
Virginia	4
Wisconsin	9
Vincent's infection:	
North Dakota	9
Whooping cough:	
North Dakota	164
Puerto Rico	134
Vermont	117
Virginia	478
Wisconsin	1,377

PLAGUE INFECTION IN CALIFORNIA, NEW MEXICO, AND WYOMING

IN A GROUND SQUIRREL AND IN FLEAS FROM GROUND SQUIRRELS IN SAN BERNARDINO COUNTY, CALIF.

Under date of August 29, 1938, Dr. W. M. Dickie, Director of Public Health of California, reported plague infection proved in one *fisheri* squirrel collected July 20, 6 miles east of Seven Oaks, San

Bernardino County, and in a pool of 84 fleas collected August 8 from 52 *fisheri* squirrels from the Crestline Public Dump, 2 miles northeast of Crestline, San Bernardino County.

IN PRAIRIE DOGS AND IN POOLS OF FLEAS FROM PRAIRIE DOGS IN CATRON COUNTY, N. MEX.

Under date of August 27, 1938, Senior Surg. C. R. Eskey reported plague infection proved in prairie dogs (*Cynomys gunnisoni zuniensis*) and in pools of fleas from prairie dogs in Catron County as follows:

In a pool of 8 fleas from 1 prairie dog found dead August 12, 6 miles north of Adams Diggings; in tissue from 2 prairie dogs shot August 12, 7 miles northwest of Adams Diggings; in a pool of 81 fleas from 3 prairie dogs shot August 13, 4 miles northwest of Adams Diggings; in a pool of 90 fleas from 12 prairie dogs shot August 16, 6 miles northeast of Adams Diggings; and in a pool of 157 fleas from 25 prairie dogs shot August 18, 6 miles south of Adams Diggings.

IN TICKS FROM GROUND SQUIRRELS IN LINCOLN COUNTY, WYO.

Under date of August 27, 1938, Senior Surg. C. R. Eskey reported plague infection proved in a pool of 9 ticks collected from 16 *C. armatus* shot July 30, 1938, 3 miles southeast of Kemmerer.

CASES OF VENEREAL DISEASES REPORTED FOR JUNE 1938

These reports are published monthly for the information of health officers in order to furnish current data as to the prevalence of the venereal diseases. The figures are taken from reports received from State and city health officers. They are preliminary and are therefore subject to correction. It is hoped that the publication of these reports will stimulate more complete reporting of these diseases.

Reports from States

	Syphilis		Gonorrhea	
	Cases reported during month	Monthly case rates per 10,000 population	Cases reported during month	Monthly case rates per 10,000 population
Alabama [1]				
Arizona [1]				
Arkansas	1,473	7.19	328	1.60
California	2,335	3.79	1,514	2.46
Colorado	148	1.38	91	.85
Connecticut [1]				
Delaware	299	11.46	50	1.92
District of Columbia	271	4.32	233	3.72
Florida [2]	1,658	9.93		
Georgia	2,589	8.39	349	1.13
Idaho	34	.69	14	.28
Illinois [2]	2,309	2.93	1,191	1.51
Indiana	425	1.22	150	.43
Iowa [2]	276	1.08	197	.77
Kansas	325	1.74	90	.48
Kentucky	796	2.73	421	1.44
Louisiana	1,363	6.39	116	.54
Maine	44	.51	67	.78
Maryland	1,350	8.04	293	1.75
Massachusetts	412	.93	337	.76
Michigan	1,257	2.60	532	1.10
Minnesota	301	1.13	176	.66
Mississippi	2,786	13.77	2,425	11.99
Missouri	1,086	2.72	260	.65
Montana [2]	33	.61	21	.39
Nebraska	73	.54	84	.62
Nevada	26	2.57	7	.69
New Hampshire	23	.45	12	.24

See footnotes at end of table.

Reports from States—Continued

	Syphilis		Gonorrhea	
	Cases reported during month	Monthly case rates per 10,000 population	Cases reported during month	Monthly case rates per 10,000 population
New Jersey	1,068	2.46	271	.62
New Mexico	123	2.91	23	.55
New York	5,983	4.62	2,037	1.57
North Carolina	3,978	11.39	719	2.06
North Dakota	23	.33	20	.28
Ohio	1,153	1.71	331	.49
Oklahoma	346	1.36	261	1.02
Oregon	96	.93	139	1.35
Pennsylvania [3]	1,449	1.42	194	.19
Rhode Island	122	1.79	55	.81
South Carolina [1]				
South Dakota	31	.45	31	.45
Tennessee	1,147	3.96	364	1.26
Texas	664	1.08	297	.48
Utah	25	.48	39	.75
Vermont	13	.34	31	.81
Virginia	992	3.67	265	.98
Washington	230	1.39	210	1.27
West Virginia [1]				
Wisconsin	67	.23	120	.41
Wyoming [1]				
Total	39,199	3.26	14,365	1.19

Reports from cities of 200,000 population or over

Akron, Ohio [1]				
Atlanta, Ga	439	15.29	107	3.73
Baltimore, Md	882	10.69	185	2.24
Birmingham, Ala	396	14.03	54	1.91
Boston, Mass	150	1.90	110	1.39
Buffalo, N. Y	121	2.04	49	.83
Chicago, Ill.[1]				
Cincinnati, Ohio	258	5.54	84	1.80
Cleveland, Ohio	233	2.50	62	.67
Columbus, Ohio	93	3.04	11	.36
Dallas, Tex	274	9.46	93	3.21
Dayton, Ohio	41	1.95		
Denver, Colo.[1]				
Detroit, Mich	624	3.60	230	1.33
Houston, Tex.[1]				
Indianapolis, Ind	22	.58	18	.48
Jersey City, N. J	124	3.85	35	1.09
Kansas City, Mo	94	2.23	3	.07
Los Angeles, Calif	677	4.73	372	2.60
Louisville, Ky	303	9.35	138	4.26
Memphis, Tenn	345	12.92	70	2.62
Milwaukee, Wis.[4]				
Minneapolis, Minn	83	1.71	53	1.09
Newark, N. J	347	7.49	127	2.74
New Orleans, La.[1]				
New York, N. Y	4,388	6.01	1,392	1.91
Oakland, Calif	65	2.14	46	1.52
Omaha, Nebr	41	1.86	42	1.91
Philadelphia, Pa	515	2.59		
Pittsburgh, Pa	411	6.01	34	.50
Portland, Oreg	8	.25	12	.38
Providence, R. I.[1]				
Rochester, N. Y	41	1.22	52	1.54
St. Louis, Mo	452	5.41	145	1.73
St. Paul, Minn	58	2.06	16	.57
San Antonio, Tex	95	3.78	67	2.67
San Francisco, Calif	235	3.50	158	2.36
Seattle, Wash	103	2.71	85	2.24
Syracuse, N. Y.[1]				
Toledo, Ohio [1]				
Washington, D. C.[5]	271	.43	233	.37

[1] No report for current month.
[3] Incomplete.
[3] Only cases of syphilitis in the infectious stage are reported.
[4] No report during present fiscal year.
[5] Reported by Social Hygiene Clinic.

WEEKLY REPORTS FROM CITIES

City reports for week ended Aug. 27, 1938

This table summarizes the reports received weekly from a selected list of 140 cities for the purpose of showing a cross section of the current urban incidence of the communicable diseases listed in the table.

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Data for 90 cities:											
5-year average	103	42	13	200	282	260	3	349	95	1,066	----
Current week	74	28	11	122	272	202	3	339	95	1,875	----
Maine:											
Portland	1	----	0	0	2	0	0	0	0	0	28
New Hampshire:											
Concord	0	----	0	0	0	0	0	1	0	0	14
Manchester	0	----	0	0	0	0	0	0	0	0	11
Nashua	0	----	0	0	0	0	0	0	0	0	8
Vermont:											
Barre	0	----	0	0	0	0	0	0	0	0	2
Burlington	0	----	0	0	0	0	0	0	0	0	8
Rutland	0	----	0	0	0	0	0	0	0	0	8
Massachusetts:											
Boston	0	----	0	3	9	10	0	9	8	28	172
Fall River	0	----	0	0	1	0	0	2	2	2	28
Springfield	0	----	0	2	1	0	0	1	0	1	22
Worcester	0	----	0	0	5	2	0	0	0	4	55
Rhode Island:											
Pawtucket	0	----	0	0	0	0	0	0	2	0	11
Providence	0	----	0	3	0	0	0	1	0	18	45
Connecticut:											
Bridgeport	0	----	0	0	0	0	0	2	0	3	22
Hartford	0	----	0	0	0	1	0	0	0	3	29
New Haven	0	----	0	0	0	0	0	0	0	29	20
New York:											
Buffalo	1	----	0	4	6	2	0	5	0	34	113
New York	6	3	1	32	53	16	0	65	28	407	1,200
Rochester	0	----	0	3	3	0	0	1	0	7	45
Syracuse	0	----	0	4	0	1	0	0	0	7	31
New Jersey:											
Camden	1	----	0	0	0	1	0	2	0	1	22
Newark	1	----	0	2	0	6	0	3	0	85	77
Trenton	0	----	0	0	0	2	0	3	0	4	39
Pennsylvania:											
Philadelphia	0	----	0	2	12	11	0	19	3	78	417
Pittsburgh	4	1	1	1	2	12	0	9	2	26	118
Reading	3	----	0	0	0	0	0	1	0	2	38
Scranton	0	----	----	0	----	0	0	----	0	4	----
Ohio:											
Cincinnati	2	----	1	0	10	3	0	8	0	7	130
Cleveland	1	1	0	4	5	5	0	8	0	83	144
Columbus	0	----	0	1	3	1	0	4	0	0	70
Toledo	0	1	1	1	2	7	0	4	1	16	72
Indiana:											
Anderson	0	----	0	0	0	1	0	0	0	3	9
Fort Wayne	0	----	0	0	0	0	0	2	0	0	19
Indianapolis	0	----	0	3	3	4	1	6	0	10	102
Muncie	0	----	0	0	0	3	0	0	0	0	10
South Bend	0	----	0	0	0	0	0	0	0	0	12
Terre Haute	0	----	0	0	0	3	0	0	0	0	13
Illinois:											
Alton	0	----	0	0	0	0	0	0	4	0	7
Chicago	6	3	1	3	21	23	0	35	5	371	597
Elgin	0	----	0	0	1	0	0	0	0	0	5
Moline	0	----	1	1	0	0	0	0	0	1	6
Springfield	0	----	0	0	0	0	0	0	0	0	23
Michigan:											
Detroit	4	----	2	4	6	9	0	19	3	198	213
Flint	0	----	0	1	1	6	0	2	0	6	16
Grand Rapids	0	----	0	0	0	6	1	0	0	2	23
Wisconsin:											
Kenosha	0	----	0	0	0	2	0	0	0	3	6
Madison	0	----	0	1	0	4	0	0	0	3	24
Milwaukee	0	----	0	0	2	3	0	3	0	190	66
Racine	0	----	0	1	0	0	0	0	0	51	7
Superior	0	----	0	0	0	1	0	0	0	0	5

City reports for week ended Aug. 27, 1938—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Minnesota:											
Duluth	0	------	0	3	1	2	0	1	1	18	15
Minneapolis	0	------	0	4	3	1	0	1	0	5	91
St. Paul	0	------	0	3	2	3	0	1	0	10	40
Iowa:											
Cedar Rapids	0	------	--------	0	-------	0	0	-------	0	1	--------
Davenport	0	------	--------	0	-------	0	0	-------	0	0	--------
Des Moines	0	------	0	0	0	3	0	0	0	0	26
Sioux City	0	------	--------	2	-------	0	0	-------	0	8	--------
Missouri:											
Kansas City	1	------	0	0	2	6	0	5	2	0	94
St. Joseph	0	------	0	0	2	0	0	2	1	1	18
St. Louis	0	------	0	0	3	6	0	9	3	10	197
North Dakota:											
Fargo	0	------	0	0	0	1	0	0	0	0	7
Grand Forks	0	------	--------	0	-------	0	0	-------	0	1	--------
Minot	0	------	0	0	0	0	0	0	0	1	9
South Dakota:											
Aberdeen	0	------	--------	0	-------	0	0	-------	0	0	--------
Sioux Falls	0	------	0	0	0	0	0	0	0	0	12
Nebraska:											
Lincoln	0	------	--------	2	-------	0	0	-------	0	7	--------
Omaha	0	------	0	1	3	0	0	1	0	0	54
Kansas:											
Lawrence	0	------	0	0	0	0	0	0	0	0	7
Topeka	0	------	0	1	1	0	0	0	1	5	--------
Wichita	0	------	0	0	0	0	0	1	0	2	23
Delaware:											
Wilmington	1	------	0	0	1	0	0	0	0	2	33
Maryland:											
Baltimore	1	2	0	7	7	0	0	10	2	19	181
Cumberland	0	------	0	0	1	0	0	0	0	0	10
Frederick	0	------	0	0	0	0	0	0	0	0	1
Dist. of Columbia:											
Washington	0	------	0	2	8	5	0	6	7	7	139
Virginia:											
Lynchburg	0	------	0	0	0	0	0	1	1	2	10
Norfolk	0	------	0	0	1	0	0	1	0	0	27
Richmond	1	------	0	1	3	4	0	4	1	0	38
Roanoke	1	------	0	0	0	0	0	1	0	0	14
West Virginia:											
Charleston	0	------	0	0	2	0	0	0	0	0	23
Huntington	0	------	--------	0	-------	0	0	-------	4	0	--------
Wheeling	0	------	0	0	1	0	0	1	1	1	17
North Carolina:											
Gastonia	0	------	--------	0	-------	0	0	-------	0	0	--------
Raleigh	0	------	0	0	1	0	0	0	0	3	19
Wilmington	0	------	1	0	1	0	0	0	0	0	11
Winston-Salem	2	------	0	0	0	1	0	1	0	2	5
South Carolina:											
Charleston	0	2	0	0	2	0	0	1	1	0	33
Florence	0	------	0	0	0	0	0	0	0	0	7
Greenville	0	------	0	0	0	1	0	0	0	1	11
Georgia:											
Atlanta	5	3	0	0	6	4	0	6	3	13	87
Brunswick	0	------	0	0	0	0	0	0	0	3	4
Savannah	2	1	0	0	0	0	0	3	1	0	27
Florida:											
Miami	1	------	0	0	1	0	0	2	1	2	36
Tampa	1	------	0	0	3	1	0	2	0	4	19
Kentucky:											
Ashland	0	------	--------	0	-------	0	0	-------	1	0	--------
Covington	0	------	0	0	1	4	0	1	0	0	17
Lexington	0	------	0	1	0	0	0	2	0	1	21
Louisville	3	1	0	2	2	0	0	2	0	3	59
Tennessee:											
Knoxville	1	------	0	0	4	0	0	0	0	2	21
Memphis	2	------	0	0	4	2	0	4	0	3	59
Nashville	0	------	0	0	0	0	0	2	0	5	40
Alabama:											
Birmingham	0	2	0	0	3	0	0	6	3	0	85
Mobile	0	------	0	0	1	0	0	0	1	0	24
Montgomery	0	------	--------	0	-------	0	0	-------	0	4	--------

City reports for week ended Aug. 27, 1938—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Arkansas:											
Fort Smith	1			0		0	0		2	0	
Little Rock	0		0	0	1	1	0	0	0	0	3
Louisiana:											
Lake Charles	0		0	0	2	0	0	0	0	0	7
New Orleans	6	3	2	1	23	1	0	14	2	15	211
Shreveport	0		0	0	3	0	0	1	0	0	42
Oklahoma:											
Oklahoma City	0		0	0	1	5	0	1	0	0	24
Tulsa	1			0		0	0		1	1	
Texas:											
Dallas	5		0	0	2	2	0	3	0	4	54
Fort Worth	1		0	0	2	0	0	2	0	0	43
Galveston	0		0	0	2	0	0	0	1	0	20
Houston	5		0	0	1	2	0	5	4	0	69
San Antonio	0		0	1	3	0	0	2	0	1	49
Montana:											
Billings	0		0	0	0	1	1	1	0	6	10
Great Falls	0		0	0	0	0	0	0	0	5	11
Helena	0		0	0	0	0	0	0	0	0	3
Missoula	0		0	0	0	0	0	0	0	0	2
Idaho:											
Boise	0		0	0	0	0	0	1	0	0	12
Colorado:											
Colorado Springs	0		0	0	0	0	1	2	0	6	7
Denver	5		0	1	7	4	0	1	0	19	67
Pueblo	0		0	1	1	0	0	0	0	3	9
New Mexico:											
Albuquerque	0		0	0	0	0	0	2	0	0	11
Utah:											
Salt Lake City	0		0	0	0	1	0	0	0	5	20
Washington:											
Seattle	0		0	0	1	0	0	2	0	13	88
Spokane	0		0	0	1	0	0	1	5	1	29
Tacoma	0		0	0	0	0	0	0	0	3	30
Oregon:											
Portland	0		0	2	1	0	1	2	0	1	68
Salem	0	3		0		1	0		0	0	
California:											
Los Angeles	6	6	0	10	8	17	0	15	2	6	263
Sacramento	0		0	3	1	1	0	0	0	5	19
San Francisco	0	1	0	10	3	6	0	5	0	14	161

State and city	Meningitis, meningococcus		Poliomyelitis cases
	Cases	Deaths	
Rhode Island:			
Pawtucket	0	0	1
New York:			
New York	0	0	4
New Jersey:			
Newark	0	0	1
Pennsylvania:			
Pittsburgh	0	0	1
Reading	1	0	0
Ohio:			
Cincinnati	0	0	1
Illinois:			
Chicago	4	0	2
Michigan:			
Detroit	1	0	1
Wisconsin:			
Milwaukee	1	0	1
Minnesota:			
Duluth	0	0	1
District of Columbia:			
Washington	0	0	2
Virginia:			
Norfolk	0	0	1
Richmond	0	0	1
Roanoke	0	1	0
North Carolina:			
Winston-Salem	1	0	0
Tennessee:			
Memphis	1	0	1
Montana:			
Great Falls	0	0	5

Encephalitis, epidemic or lethargic.—Cases: Kansas City, Mo., 1; St. Louis, 2; Minot, 5; Omaha, 1; Lawrence, Kans., 1; Birmingham, 1; Denver, 2.

Pellagra.—Cases: Winston-Salem, 2; Atlanta, 6; Savannah, 3; Knoxville, 1; Montgomery, 2.

Typhus fever.—Cases: Cleveland, 1; Norfolk, 1; Charleston, S. C., 9; Savannah, 1; Tampa, 1; Galveston, 1; Houston, 3. Deaths: Charleston, S. C., 1.

FOREIGN AND INSULAR

JAPAN

Poliomyelitis.—According to information dated August 6, 1938, a severe epidemic of poliomyelitis has broken out in the Hanshin (Osaka–Kobe) area of Japan. In recent weeks more than 500 cases have been reported, almost invariably attacking children mostly under 3 years of age, while adults seem to be almost completely immune. The mortality rate is said to be very low.

LATVIA

Notifiable diseases—April–June 1938.—During the months of April, May, and June 1938, cases of certain notifiable diseases were reported in Latvia as follows:

Disease	April	May	June	Disease	April	May	June
Botulism	3	3	8	Mumps	235	205	144
Cerebrospinal meningitis	9	13	3	Paratyphoid fever	6	9	10
Diphtheria	102	87	94	Poliomyelitis	12	14	6
Dysentery	6	----	----	Puerperal septicemia	11	13	10
Erysipelas	41	64	45	Scarlet fever	420	366	209
Influenza	97	274	91	Smallpox	----	1	----
Lead poisoning	----	----	1	Tetanus	1	1	3
Leprosy	----	2	2	Trachoma	71	43	64
Lethargic encephalitis	1	1	----	Tuberculosis	317	375	333
Malaria	1	----	----	Typhoid fever	44	38	41
Measles	11	56	30	Whooping cough	210	135	131

YUGOSLAVIA

Communicable diseases—4 weeks ended August 14, 1938.—During the 4 weeks ended August 14, 1938, certain communicable diseases were reported in Yugoslavia as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Anthrax	100	3	Paratyphoid fever	34	----
Cerebrospinal meningitis	13	4	Poliomyelitis	2	----
Diphtheria and croup	319	21	Scarlet fever	130	3
Dysentery	295	17	Sepsis	9	----
Erysipelas	137	5	Tetanus	56	19
Favus	5	2	Typhoid fever	291	19
Leprosy	1	----	Typhus fever	23	1
Lethargic encephalitis	1	----			

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

NOTE.—A table giving current information of the world prevalence of quarantinable diseases appeared in the PUBLIC HEALTH REPORTS for August 26, 1938, pages 1544–1558. A similar cumulative table will appear in future issues of the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

China.—During the week ended August 27, 1938, cases of cholera were reported in China as follows: Canton, 6; Hong Kong, 21; Macao, 41; Shanghai, 586; Swatow, 7.

Indochina (French)—Annam Province.—During the week ended August 27, 1938, 75 cases of cholera were reported in Annam Province, French Indochina.

Plague

Peru—Lima Department—Sayan.—For the period July 1–31, 1938, one fatal case of plague was reported in Sayan, Lima Department, Peru.

United States.—A report of plague infection in California, New Mexico, and Wyoming, appears on pages 1676 and 1677 of this issue of PUBLIC HEALTH REPORTS.

Yellow Fever

Brazil—Amazonas State—Coary.—On July 24, 1938, one death from yellow fever was reported in Coary, Amazonas State, Brazil.

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